Clinical Predictors of Stroke Mimics in Patients Treated with Recombinant Tissue Plasminogen Activator according to a Normal Multimodal Computed Tomography Imaging

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Background: Multimodal computed tomography imaging (MCTI) is increasingly used for rapid assessment of acute stroke. We investigated characteristics and final diagnoses of patients treated with recombinant tissue plasminogen activator (rt-PA) while admission imaging was unremarkable. *Methods:* From our prospectively collected stroke database (2013-2016), we identified consecutive patients treated with rt-PA on the basis of an unremarkable brain MCTI and assessed with a 24-hour follow-up brain magnetic resonance imaging (MRI). Demographic data, medical history, score on the 15-item National Institute of Health Stroke Scale, and final diagnosis were considered. Absence of MRI infarction and alternate diagnosis defined stroke mimics (SMs). Univariable and multivariable logistic regression analyses identified factors predictive of SMs. *Results:* Sixty-eight (47.9%) SMs, 63 (44.4%) strokes, and 11 (7.7%) aborted strokes were found. SMs had more often aphasia ($P = .003$) and hemianopia ($P = .0008$), whereas upper limb weakness (ULW) ($P = .03$) and limb ataxia ($P = .002$) were more prevalent in strokes. Headache (adjusted odds ratio [Adj. OR], 3.89 [95% confidence interval {CI} 1.44-10.47]), relevant history of epilepsy, migraine, dementia or depression (Adj. OR 3.66 [95% CI 1.31-10.18]), unilateral sensory loss (Adj. OR 2.60 [95% CI 1.05-6.45]), and hemianopia (Adj. OR 4.94 [95% CI 1.46-16.77]) were independent predictors of SMs whereas ULW (Adj. OR 3.16 [95% CI 1.28-7.82]) and ataxia (Adj. OR 3.81 [95% CI 1.43-10.13]) predicted stroke. Sensitivity of hemianopia or aphasia for SMs was 52.9%, with specificity of 84.1%, positive predictive value of 78.3%, and negative predictive value of 62.4%. *Conclusions:* Hemianopia and/or aphasia with normal MCTI suggest SMs. Diffusion-weighted MRI might be discussed before rt-PA administration in patients with such a clinical pattern. **Key Words:** Stroke mimics—multimodal CT imaging—thrombolysis—safety.
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Introduction

Stroke patients require rapid assessment and triage to improve access to thrombolytic therapies and endovascular procedure.[1] Earliest treatment and recanalization are strongly associated with favorable outcomes.[2] However, shortening door-to-needle time may result in inadvertent intravenous thrombolysis treatment in stroke mimics (SMs). Indeed, SMs have been estimated up to 16.7% of patients treated with thrombolysis.[3-7] Whereas magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT)[8] to provide evidence of infarction within the first hours from the onset, CT is still the most frequent imaging modality used in the initial assessment of stroke code patients. Compared with MRI, CT is widely available with rapid imaging acquisition, easy to manage in unstable patients and well tolerated in those who suffer from claustrophobia. Besides noncontrast CT, multimodal CT imaging (MCTI), including brain CT, CT angiography (CTA) to assess artery patency, and CT perfusion (CTP) map to detect infarction core and penumbra, is now increasingly available. Whereas MCTI improves diagnostic accuracy for acute ischemic stroke,[9,10] one third of infarcts are undetected regarding their small size or their localization outside the volume of perfusion map coverage.[11] Studies suggest that thrombolysis in SMs is safe[12-16] and normal initial imaging in patients with clinical features suggestive of stroke should not preclude the intravenous administration of recombinant tissue plasminogen activator (rt-PA).[6]

The aim of our observational study was to assess characteristics and final diagnosis for patients treated with rt-PA within 4.5-hour while initial MCTI was unremarkable.

Patients and Methods

Study Design and Population

The present retrospective study was conducted in the stroke unit of the University Hospital of Bordeaux between January 1, 2013, and June 30, 2016.

Patients were identified from our stroke database, which collects each medical record prospectively. Consecutive patients were selected on the basis of the following criteria: (1) patients admitted for sudden and focal clinical symptoms suggestive of acute stroke, (2) brain MCTI performed within 4 hours of stroke onset and interpreted as unremarkable by both the radiologist and the stroke neurologist in charge of the patient, (3) administration of intravenous rt-PA within 4.5 hours, (5) brain MRI performed at 24 hours of the thrombolysis treatment, and (6) availability of clinical follow-up until patient discharge. No detection by both the radiologist and the neurologist of perfusion defect on CTP and no arterial occlusion on CTA defined an unremarkable MCTI.

Demographic data, relevant medical history, vascular risk factors, treatment and pre-admission modified Rankin Scale scores were carefully collected. Relevant medical histories of dementia, seizure, migraine, depression, and anxiety were considered in this study. Total score and 15-item subscore of the National Institute of Health Stroke Scale (NIHSS) were systematically calculated at admission, at 24 hours, and at hospital discharge. Each subscore of the NIHSS was considered for the analysis.

A systematic blood laboratory work-up was performed before rt-PA administration.

Imaging Protocol and Imaging Analysis

Patients admitted with stroke code activation are routinely investigated by brain CT, cervical and intracranial arteries CTA, and CTP. Images were performed on a 64-slice CT (General Electric Optima 660, General Electric, Chicago, IL). CTP source images were loaded on an advantage workstation Volume Share 5 (General Electric Healthcare, General Electric, Chicago, IL). Perfusion maps were automatically generated and disclosed time to peak (TTP), mean transit time (MTT), cerebral blood volume (CBV), and cerebral blood flow (CBF) maps. Emergency MCTI assessment was the result of a consensual analysis between the radiologist and the stroke neurologist who were in charge of the patient.

A systematic 24-hour 3T brain MRI was performed after rt-PA administration including diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC), fluid-attenuated inversion recovery, gradient-echo, and time-of-flight sequences. Infarction was defined as a high signal on DWI sequences associated with a low signal on ADC sequences. Each infarction was characterized by its artery territory localization. Subcortical infarctions less than or equal to 20 mm on DWI sequences were defined as lacunar infarction.

All the sequences were analyzed for differential diagnosis of stroke.

Follow-up and Final Diagnosis

All patients treated with rt-PA are reviewed with additional tests in our outpatient department between 3 and 6 months after hospital discharge. The stroke team at the end of this final medical examination establishes the final diagnosis.

Patients were divided into two groups. The presence of a cerebral infarction lesion on the 24-hour brain MRI classified the patient into the stroke group, whereas the absence of cerebral infarction lesion associated with an alternate diagnosis at the end of clinical follow-up classified the patient into the SM group. Patients who did not show cerebral infarction on 24-hour brain MRI without any alternate diagnosis than possible aborted stroke were excluded from the analysis.