Distance to Thrombus in Acute Middle Cerebral Artery Occlusion Predicts Target Mismatch and Ischemic Penumbra

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Background and Purpose: In patients with occlusion of the middle cerebral artery (MCA) treated by intravenous thrombolysis (IVT), the distance to thrombus (DT) has been proposed as a predictor of outcome. The purpose of the present study was to investigate how DT relates to dynamic susceptibility contrast perfusion metrics. *Methods:* Retrospective analysis was undertaken of patients who were diagnosed with acute MCA occlusion by magnetic resonance imaging and treated with IVT. Volumes of time-to-maximum (Tmax) perfusion deficits and diffusion-weighted imaging (DWI) lesions, diffusion–perfusion mismatch volumes, and the presence of target mismatch were determined. Correlations between the above stoke measures and DT were then calculated. *Results:* Fifty-five patients were included. DT showed significant inverse correlations with Tmax greater than 4, 6, 8, and 10 seconds, respectively, and mismatch volumes. Using the DT group median (14 mm) as a separator, significant intergroup differences were observed for Tmax greater than 4, 6, and 8 seconds, respectively, and for mismatch volumes. Grouping DT into quartiles showed significant intergroup differences regarding mismatch volumes and Tmax values greater than 4 and 6 seconds. Binary logistic regression identified DT (odds ratio [OR] = .89; 95% confidence interval [CI], .81-.99) and DWI lesion volumes (OR = .92; 95% CI, .86-.97) as independent predictors of target mismatch. A low DT predicted target mismatch with an area under the curve of .69. *Conclusions:* DT correlates inversely with Tmax perfusion deficits and mismatch volumes and acts as an independent predictor of target mismatch.
Key Words: Magnetic resonance angiography—perfusion imaging—diffusion-weighted imaging—stroke—distance to thrombus.

Introduction

Treatment for patients with an acute stroke due to an intracranial large vessel occlusion has moved away from intravenous thrombolysis (IVT) over the past few years, with current trends preferring mechanical thrombectomy (MT). While several trials failed to show MT superiority initially,[1-3] recent multicenter studies applying new imaging and treatment techniques favor MT over IVT.[4-8] In two of these trials, perfusion imaging studies were routinely performed for patient selection.[6,7] The presence of a mismatch between infarct core and penumbra is thought to be crucial if patients were to benefit from reperfusion, whether by IVT or MT.[9,10] Although publications on this topic are rare, it is known that penumbral

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volumes and the collateral circulation depend strongly on clot location. Furthermore, since clot location is a predictor of patient outcome[11-13] determining the precise localization of the occlusion site in acute stroke is paramount for clinical decision making.[14]

To determine the exact thrombus localization in acute middle cerebral artery (MCA) occlusions, a new analysis parametric, called the distance to thrombus (DT), has been established.[15,16] The DT is an easy-to-apply measurement of the length from the carotid T to the occlusion site in MCA stroke, which can be determined by computed tomography (CT) angiography or magnetic resonance angiography (MRA). DT has also been shown to be a predictor of individual patient outcome[15,16] and might help avoid the need for classical categorical separation of MCA segments, whose exact boundaries are frequently difficult to define.

The purpose of the present study was to elucidate how DT relates to dynamic susceptibility contrast (DSC) perfusion metrics, in particular with regard to diffusion–perfusion mismatch or target mismatch.

Methods

Study Population

This study was approved by the institutional ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Due to the study's retrospective nature, the ethics committee waived informed consent.

All patients with a diagnosis of an acute ischemic stroke from January 1, 2009, to December 31, 2013, who underwent magnetic resonance imaging (MRI) before onset of IVT were identified for inclusion, and data were prospectively collected. A retrospective analysis was performed. Inclusion criteria were (1) evidence of an acute diffusion restriction on the b1000 images and correspondingly on the apparent diffusion coefficient map in the territory of the MCA, and (2) a proven occlusion of the MCA by means of contrast-enhanced (CE)-MRA in the M1 or M2 segment. National Institutes of Health Stroke Scale (NIHSS) scores were recorded at patient admission and data on hypertension, diabetes, atrial flutter/fibrillation, and hyperlipidemia were collected.

Patient Characteristics

Altogether, 605 patients underwent IVT for the treatment of acute ischemic stroke at our tertiary care university hospital. Of these patients, 169 underwent MRI as the primary imaging method; 143 were diagnosed with an acute diffusion lesion in the anterior circulation of which 64 were diagnosed with an occlusion of the MCA in the M1 or M2 segment. In 3 patients, measurement of the DT was not possible because of motion artifacts or an occlusion too distally located to be measurable on maximum intensity projection reconstructions of CE-MRA source images. Of the remaining 61 patients, 6 did not undergo DSC perfusion or the raw data were of insufficient quality for the purposes of this investigation. Thus, 55 patients remained for further analysis. Patient characteristics regarding DT, diffusion-weighted imaging (DWI) lesion volumes, time-to-maximum (Tmax) lesion volumes, mismatch, hypoperfusion intensity ratio (HIR), baseline NIHSS score, and other factors are detailed in Table 1.

Table 1. *Patient characteristics presented as proportions or as median with IQR and range, if appropriate*

Parameter	Value
Age	79.0 years (IQR 14.0), 27-96
Male sex	24 (43.6%)
Left hemisphere stroke	35 (63.6%)
Onset to IV rt-PA	145.0 min (IQR 55.0), 75-270
Distance to thrombus	14.0 mm (IQR 12.0), 3-52
DWI lesion volume	15.7 mL (IQR 26.6), .7-107.4
Tmax greater than 4 s	141.6 mL (IQR 94.6), 26.7-313.1
Tmax greater than 6 s	81.3 mL (IQR 63.7), 10.0-219.0
Tmax greater than 8 s	52.2 mL (IQR 51.5), 1.8-151.5
Tmax greater than 10 s	29.7 mL (IQR 40.4), .2-116.6
Mismatch volume	59.0 mL (IQR 69.5), −40.2-176.0
Mismatch ratio	4.2 (IQR 7.7), .4-133.0
Hypoperfusion intensity ratio	.4 (IQR .3), 1.7-75.7
Target mismatch present	39 (74.5%)
Hypertension	39 (70.9%)
Atrial fibrillation	11 (20.0%)
Hyperlipidemia	10 (18.2%)
Diabetes mellitus	17 (30.9%)
NIHSS score at admission	12.0 (IQR 9.0), 0-24

Abbreviations: DWI, diffusion-weighted imaging; IQR, interquartile range; IV, intravenous; NIHSS, National Institutes of Health Stroke Scale; rt-PA, recombinant tissue plasminogen activator; Tmax, time to maximum.

MRI

Imaging was performed on a 3T scanner (Siemens Trio; Siemens Healthcare, Erlangen, Germany) or 3 different 1.5 T magnetic resonance (MR) scanners (Gyroscan Intera and Achieva; Philips Healthcare, Best, The Netherlands; and Magnetom Symphony, Siemens Healthcare). The department's standardized stroke protocol consisted of axial DWI, axial fluid-attenuated inversion recovery (FLAIR), axial gradient echo (T2* at 1.5 T and susceptibility-weighted imaging at 3 T), DSC perfusion imaging, intracranial time-of-flight angiography, and intracranial/extracranial CE-MRA. For CE-MRA, a coronally oriented