The Utility of Middle Cerebral Artery Clot Density and Burden Assessment by Noncontrast Computed Tomography in Acute Ischemic Stroke Patients Treated with Thrombolysis

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Background: Quantitative and qualitative evaluation of middle cerebral artery (MCA) density, together with extent of thrombi, was assessed on plain computerized tomography (CT) to delineate better the prognostic value of the hyperdense MCA sign (HMCAS) in a cohort of patients who underwent intravenous or intra-arterial thrombolysis. *Methods:* Density of MCA was quantified by maximum pixel-sized measurement of Hounsfield unit (HU) in 105 patients with acute MCA proximal segment occlusion, 15 patients with vertebrobasilar circulation stroke (VBS) and 44 nonstroke control subjects. Predictive value of HMCAS, absolute HU value of within MCA, side-to-side HU ratio, and difference along with a newly introduced hyperdense MCA burden score in early dramatic recovery (EDR) and third-month favorable prognosis were determined with multivariate adjustment for age, baseline stroke severity, and thrombus length as measured on CT angiography. Receiver operator characteristics (ROC) curves were used to determine the cutoffs of quantitative indices to determine HMCAS and their prognostic significance. *Results:* Higher HU was present in the ipsilateral MCA of the patients compared with their contralateral side and basilar tip and any MCA of VBS stroke and control subjects (area under the curve [AUC] of ROC curves was .753). Symptomatic-to-asymptomatic HU difference and ratio of MCA stroke were also significantly higher than side-to-side difference calculated in VBS stroke and control groups (AUC of ROC curves: .770 and .764, respectively). Optimal thresholds of absolute HU (44), side-to-side HU difference (2), and ratio (1.0588) showed borderline sensitivity and specificity. HMCAS and its quantitative indices were not significantly associated with EDR and favorable third-month outcome. Furthermore, there was no difference in terms of cardioembolic and atherothrombotic thrombi HU. *Conclusions:* Utility of the HMCAS as a prognostic marker in stroke thrombolysis is not high in the CT angiography era. Previous observation regarding its positive prognostic role can be attributed to its association with proximal location and extent of clot burden, which are detectable reliably with current CT angiography techniques. Neither quantification nor extent of increased density seems to have clinical utility for treatment decision making in MCA strokes and prediction of emboli composition and response to recanalization attempt. **Key Words:** Hounsfield unit—middle cerebral artery—stroke—computerized tomography—attenuation—prognosis.

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Introduction

Despite increasing availability of magnetic resonance imaging (MRI), noncontrast computed tomography (CT) continues to be the imaging modality of choice in acute stroke care in many institutions. Actually, CT-based modern stroke imaging protocols incorporating CT perfusion and CT angiography fulfill most of the requirements for management of hyperacute stroke, such as detection of early signs of parenchymal ischemia, extent of perfusion deficit, and vascular status including location of occluding thrombus. The other 2 required issues regarding acute stroke management, albeit still not fully accomplished by available CT and/or MRI techniques, are the determination of the composition and volume of occluding thrombi.

For the first issue—prediction of clot composition—the hyperdense artery sign on CT and hypointense vessel sign on T2* or susceptibility-weighted MRI have been proposed to be useful. Using histopathologic confirmation from acutely retrieved thrombotic material, a recent study showed that hyperdense/hypointense vessels signs on imaging reflect red blood cell content of the thrombi.[1] More indirectly, quantified density (Hounsfield unit [HU]) of an occluding thrombus on CT has been suggested to be discriminative of artery-to-artery cerebral embolism from cardiogenic ones, in other words, presumably white and red thrombi, respectively, in 1 study[2]; however, this observation could not be replicated by others.[3] In addition to this ambiguity, potential diagnostic and therapeutic implications of exploring the clot structure with HU quantification on prethrombolysis CT have led us to revisit not only quantitative but also qualitative aspects of the hyperdense middle cerebral artery sign (HMCAS) to clarify their clinical utility in the setting of acute stroke thrombolysis.

For the second issue—prediction of the extent of obstructing thrombus—direct measurement of intra-arterial clot length and use of several semiquantitative scores on cerebral angiography studies, where CT angiography has recently become popular, perhaps, because of its punctual availability, were proposed.[4-5] Previous studies have shown that higher thrombus volume can negatively affect functional and final tissue outcome and increase parenchymal hematoma risk following thrombolysis.[5-7] Because of limited availability of acute angiography, a more available, simple, and practical alternative of clot burden assessment based on noncontrast CT may be advantageous in the emergency department setting. To accomplish this aim, we adapted, and then tested, a clot burden score (CBS)[5] previously described for CT angiography to noncontrast CT (the hyperdense MCA burden score [HMCABS]).

Overall, we are in search of more dependable noncontrasted (plain) CT-derived prognosticating tools for acute middle cerebral artery (MCA) stroke thrombolysis in the current CT angiography era. If plain CT gives reliable information about the extent and composition of the occluding thrombi, impact on various components of the management and decision making would be quite advantageous in terms of safety and financial aspects.

Methods

Patients

A total of 105 consecutive patients (mean ± SD age: 63.3 ± 13.4 years; 52 women and 53 men) with acute MCA M1 segment occlusion (88 proximal M1; 27 distal M1; 57 left; 47 right, 1 bilateral) who received intravenous or intra-arterial thrombolysis (intravenous recombinant tissue plasminogen activator 78; intra-arterial lysis/intervention 10; combined therapy 17) between January 2006 and December 2012 were included into the present study. In 22 patients, ipsilateral internal carotid artery (ICA) occlusion accompanied the M1 occlusion. An additional 17 patients with M1 occlusion admitted during the study period were excluded from the analyses because of various reasons: absence of pretreatment CT images (n = 9; treatment based on MRI in 4, imaging in outside hospital in 3, missing data in 2); unsatisfactory pretreatment vascular imaging (n = 3); presence of imaging confounding factors or artifacts precluding reliable quantitative and qualitative density evaluations (n = 5; and presence of intravascular contrast on baseline CT secondary to recent coronary angiography, movement artifacts, aneurysm coil, dolicoectatic artery, and dissection with hemorrhage within artery wall 1 each).

Fifteen patients (mean ± SD age: 65.4 ± 15.7 years; 6 women and 9 men) with acute vertebrobasilar occlusion (11 basilar and 4 vertebral) who also received thrombolytic treatment (intravenous recombinant tissue plasminogen activator 10; intra-arterial lysis 2; combined therapy 3) during the study period served as the "vascular control" group. Clinical, radiographic, and detailed angiographic data in these 2 groups were prospectively acquired as part of a prospective registry at our center. In addition, 44 consecutive patients (mean ± SD age: 58.5 ± 15.1 years; 22 women and 22 men) with normal findings on brain MRI and CT angiography, both obtained for diverse acute complaints at the emergency department during the year of 2011, served as the "control" group (Supplementary Table 1). The institutional ethics committee approved the study protocol.

Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS)[8] at admission, at 24 hours, and at discharge. Functional outcome was evaluated at admission, at discharge, and at the end of the third month by using modified Rankin Scale (mRS).[9] Early dramatic recovery or response to lysis was defined as a decrease of the NIHSS score to less than 4 or improvement of NIHSS score by at least 10 points at the end of the first 24 hours.[10] Late favorable outcome was defined as an mRS score of 2 or more at the end of the third month after