Prediction of Malignant Middle Cerebral Artery Infarction in Elderly Patients

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Background: We evaluated the clinical outcomes of malignant middle cerebral artery (MCA) infarction (MMI) and determined an infarcted brain volume (BV) threshold value for accurate MMI prediction in elderly patients. *Methods:* We analyzed 69 consecutive patients (mean, 75.6 ± 11.7) with internal carotid artery or MCA infarction within 48 hours from onset. Diffusion-weighted high-intensity volume (DHV) and BV were measured in all patients. The percentage of DHV within BV (DHV/BV ratio) was calculated to standardize the DHV difference for each individual BV. Patients were stratified based upon their MMI status and age, compared with the following: (1) MMI versus non-MMI groups and (2) age ≥75 years group versus age <75 years group, based on DHV values, DHV/BV ratio, Glasgow Coma Scale (GCS) scores on admission, and modified Rankin Scale (mRS) scores at 3 months after onset. *Results:* The MMI group (n = 14) showed significantly larger DHV values ($P < .001$), larger DHV/BV ratios ($P < .001$), lower GCS scores on admission ($P < .01$), and higher mRS scores at 3 months ($P < .001$) than the non-MMI group. The DHV threshold value predicting MMI was 102 cm^3 (sensitivity 85%, specificity 91%, $P < .01$) and DHV/BV threshold ratio was 7.8% (sensitivity 86%, specificity 87%, $P < .01$). Both the age ≥75 years group and the age <75 years group with MMI showed equally poor outcomes (mRS 5.7 ± .7 versus 5.3 ± 1.3). *Conclusions:* DHV and DHV/BV can provide reliable information for MMI prediction in elderly patients. **Key Words:** Middle cerebral artery occlusion—diffusion-weighted imaging—volumetry—elderly.

Introduction

Malignant middle cerebral artery (MCA) infarction (MMI) is one of the most devastating forms of ischemic stroke.[1-4] Early decompressive craniectomy has been shown to be a useful treatment procedure for MMI in previous randomized studies.[5-8] However, despite its usefulness in treating MMI, clinically attempting to predict MMI in patients with acute cerebral infarction is problematic. In the search for a useful MMI predictor, volumetry of diffusion-weighted high-intensity areas using acute magnetic resonance (MR) images has recently become a fairly reliable candidate for MMI prediction.[9,10]

As is well known, Japanese people are granted considerable longevity, and the elderly population is increasing. A recent Japanese Stroke Registry study substantiated the

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fact that the average age at initial acute ischemic stroke onset is 71.3 years.[11] The survey also revealed that the number of elderly patients with cerebral infarction has explosively increased[12] and showed a significantly higher acute death rate than that of younger patients.[1] However, until now, clinical volumetric data from diffusion-weighted MR images of elderly brains showing hyperintense areas have not been fully studied.

In the present study, to clarify the relationship between MMI and diffusion-weighted high-intensity volume (DHV) in elderly patients with cerebral infarction, we measured early DHV in 69 consecutive patients with acute ischemic stroke. We analyzed the relationship between DHV values in MMI versus non-MMI groups, and age ≥75 years group and age <75 years group, Glasgow Coma Scale (GCS) scores on admission, and modified Rankin Scale (mRS) scores at 3 months after onset. To minimize the effect of age-related brain atrophy on the volumetric analysis, we calculated a standardized DHV corresponding to each individual brain volume (BV) as the DHV/BV ratio. We then analyzed and compared the relationships between the DHV/BV ratio in a similar manner as we analyzed the DHV values.

Subjects and Methods

Patients

Between June 2007 and September 2010, a total of 516 patients with cerebral infarction were admitted to Hanwa Memorial Hospital. Of these patients, we retrospectively analyzed the data from 69 (26 men and 43 women). Inclusion criteria were as follows: (1) acute infarction with occlusion of internal carotid artery or MCA admitted within 48 hours of onset; (2) both MR imaging and conventional computed tomography (CT) scanning performed on admission; and (3) neuroprotective agents, anticoagulant drugs, antiplatelet drugs, and thrombolytic drugs used for patients who met the criteria described in the Japanese Guidelines for the Management of Stroke.[11]

All patients were admitted to the critical care unit of our stroke center and were treated according to standardized protocols. GCS scores on admission were assessed by neurosurgeons. Diagnosis of MMI was referred by the definition used in the Oppenheim's study[9] and based on clinical course and follow-up CT according to the following criteria: (1) secondary neurological deterioration including at least a decline in consciousness as defined by GCS score and (2) large space-occupying infarction including the MCA territory on follow-up CT with midline shift assessed by more than 2 neurosurgeons. Decompressive surgery was considered if the follow-up CT revealed MMI and patients fulfilled hospital criteria of prestroke mRS score of 0 or 1, with the nondominant hemisphere involved. Patients with a prestroke mRS score of 2 or higher, with fixed and dilated pupils, or with symptomatic hemorrhage in the infarcted area were excluded. All patients were cared by the team of rehabilitation experts in the hospital during the acute phase of stroke. Outcome was assessed using mRS scores at 3 months after stroke onset.

MR Imaging Protocol

MR imaging was performed with a 1.5-T scanner equipped with a 20-mT/m gradient system (Excelart XG, Toshiba Medical Systems, Tochigi, Japan). Images of diffusion-weighted, apparent diffusion coefficient, T1-weighted, T2-weighted, fluid-attenuated inversion recovery, and a time-of-flight MR angiogram (MRA) were acquired in 1 session with a standard protocol. Initial magnetic resonance imaging (MRI) was performed at the time of admission, and the MR images of all the patients were obtained within 48 hours after onset. Diffusion weighted imaging (DWI) was obtained using a multislice, single-shot, spin-echo echo planar imaging sequence, with a slice thickness of 6 mm and a 2-mm gap; number of slices included the whole brain (average of 18); matrix size, 128×128; field of view, 28×25 cm; b-value, 1000 s/mm^2; TR/TE, 8000/130 ms; diffusion-sensitizing gradient applied in 3 directions (x, y, z); and imaging time, 48 s. Site of vessel occlusion was investigated based on MRA findings.

CT Scanning Protocol

All CTs were performed with a 64-multidetector row CT scanner (Aquilion 64, Toshiba Medical Systems). The protocol consisted of a scout image and unenhanced CT from the skull base to the vertex with the gantry angle along the orbito-meatal line and 8-mm slice thickness. Initial CT was performed at the time of admission and follow-up CT was performed in the event of neurological or consciousness deterioration.

Volume Measurement and Region of interest (ROI) Analysis

A neurosurgeon (Y.G.) measured both the DHV as infarct volume and whole-brain volume on CT using digital imaging and communications in medicine (DICOM)-based image analyzing software, OsiriX (Pixmeo, Bernex, Switzerland). OsiriX can be used for these volumetric methods with accuracy.[13,14] DHV was quantitatively measured on DWI with a b-value of 1000 s/mm^2. DICOM data from DWI were sent to OsiriX and each infarcted area was displayed as a high-intensity area on each DWI slice. A cursor was initially positioned on the high-intensity area, and then the intensity threshold was progressively reduced until the total selected area matched the high-intensity area that would have been manually selected. The volume was obtained by multiplying the surface by the slice thickness plus the intersection gap. The DWI value of the unaffected hemisphere was determined in order to set the lower and upper thresholds of DWI high-intensity areas. The BV on CT was measured in a similar manner on selected brain tissue of each slice. We calculated DHV/BV (%) as in Figures 1 and 2.