An Objective Measurement of Lacunar Infarct Location from the Middle Cerebral Artery Stem

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Background: There is emerging interest in the relationship between neuroimaging location of lacunar infarcts and underlying stroke risk factors. Recent methods used for localization of lacunar infarcts are affected by high inter-rater variability. We used a novel algorithm-driven method that provided quantitative assessment of the distance of the lacunar infarct from the origins of the lenticulostriate arteries. *Methods:* We conducted a retrospective analysis of patients who presented with lacunar infarcts between 2007 and 2011. Diffusion-weighted imaging and magnetic resonance angiography were used to manually mark the infarct lesion and the ipsilateral origins of lenticulostriate arteries. A 3-dimensional distance formula computed the distance between the infarct and the arterial region of interest. All distances were adjusted for brain volumes. Agreement testing using 2 blinded assessors was used to determine reproducibility of this method. *Results:* One hundred and ten patients were included in our study, with a median age of 72 years (interquartile range 58-81); 67 (61%) were male and 33 (30%) had hypertension and other vascular risk factors including hypercholesterolemia 45 (41%), smoking 33 (30%), diabetes 24 (22%), ischemic heart disease 18 (16%), and atrial fibrillation 9 (8%). The agreement test for 33 patients demonstrated an intraclass correlation of .89 and Lin's correlation coefficient of .89 (95% confidence interval .816-.963). The median distance for the study cohort was 24.5 mm, with shorter median distances of 13.7 mm observed in patients with atrial fibrillation (P value < .005). *Conclusion:* Our study used a novel method to calculate a distance measurement, which has high inter-rater correlation. **Key Words:** Lacunar stroke—hypertension—lipohyalinosis—diffusion-weighted imaging.

Introduction

Lacunar infarcts are due to pathology in the deep, small penetrating arteries, such as the lenticulostriate arteries.[1,2] The clinical manifestations of lacunar infarcts are variable, including a range of neurologic syndromes with differing motor or sensory deficits in the absence of cortical signs.[1] The incidence of lacunar infarcts ranges from 13 in 100,000 to 59 in 100,000, and may account for up to 25% of all ischemic strokes.[3,4] Multiple stroke risk factors have been associated with lacunar infarcts including hypertension, diabetes, hypercholesterolemia, and smoking.[5,6] However, only a few studies have investigated the relationship between locality of lacunar infarcts and these risk factors.[7-10]

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Perforator artery pathology is likely the responsible mechanism for lacunar infarcts.[11] Fisher observed lipohyalinosis, a process of arterial disorganization affecting the walls of lenticulostriate arteries, which he attributed to hypertension.[12] There has been failure to replicate similar vascular pathologies in animal models.[13] Other mechanisms of lacunar infarcts include intracranial atheromatous disease affecting the proximal segments of the lenticulostriate arteries or the origins of these arteries because of occlusion by plaques in the middle cerebral artery (MCA).[14]

It has been postulated that differing occlusion sites along the perforator arteries could lead to lacunar infarcts at variable distances from the origins of the lenticulostriate arteries. Nah et al used visual inspection methods to define lacunar infarcts as distal if they did not extend to the basal surface of the parent artery.[7] They found these correlated more closely with small-vessel disease risk factors such as hypertension, suggesting lipohyalinosis as the culprit etiology. These results, however, may be subject to inter-rater bias. Therefore, there is a need for a quantitative, automated, image-processing method. The aim of this study was to assess the reproducibility and application of a novel algorithm-driven method to measure the distance between the lacunar infarct and the ipsilateral MCA stem.

Methods

Study Population

This was a single-center, retrospective study undertaken at the Royal Melbourne Hospital, Australia. Approval from the Human Research and Ethics Committee was granted. Patient data were accessed from a prospectively collected database. All consecutive patients with acute stroke who presented between 2007 and 2011 who underwent diffusion-weighted imaging (DWI) and magnetic resonance angiography (MRA) within 7 days of presentation with an anterior circulation stroke defined by the Oxfordshire Community Stroke Project Classification System as a lacunar circulation infarct (LACI) or partial anterior circulation infarct (PACI) were considered for the study.[15] Clinical classification for a LACI required hemisensory or motor deficit (proportionally involving at least 2 of face, arm, and leg) with or without ipsilateral cerebellar signs and absence of cortical and sensory features. Clinical classification of PACI required higher cerebral dysfunction alone, or with a motor or sensory deficit more restricted than those whose syndrome is classified as a LACI.

Radiological classification of a LACI included spheroidal infarct in deep white matter and basal ganglia with a maximum diameter of 15 mm, and for PACI cortical or subcortical infarcts in either MCA or anterior cerebral artery territories not meeting total anterior circulation infarct or LACI criteria.

Inclusion criteria included a visible subcortical infarct (lesion diameter <20 mm) in the lenticulostriate artery territory demonstrated on DWI with concurrent MRA or computed tomography angiography (CTA) available for subsequent neuroimaging analysis. Patients with greater than 2 lacunar infarcts suggesting a likely cardioembolic etiology and other confirmed conditions such as moyamoya disease were excluded from the study.

Patient demographics were collected. Stroke risk factors included hypertension (defined as patient currently receiving medication for hypertension or blood pressure >140/90 mm Hg on 2 or more repeated measurements), type 2 diabetes mellitus (defined as patient currently receiving medication for diabetes or abnormal fasting blood glucose >7 mmol/L or HbA1c >6.5% or >48 mmol/mol), hypercholesterolemia (defined as patient currently receiving medication for hypercholesterolemia or elevated fasting lipids with total cholesterol >5.5 mmol/L), smoking status (defined as smoker or nonsmoker), and atrial fibrillation (defined as present if confirmed on electrocardiography or Holter monitor).

Neuroimaging Analysis

All imaging was conducted at Royal Melbourne Hospital using a Siemens 1.5 Tesla magnetic resonance imaging (MRI) machine (General Electric, Parkville, Victoria). A single-shot diffusion-weighted MRI protocol was performed to acquire 27 (5-mm thick) contiguous axial images with (B0) and without (B1000) 1000 mm^2/s of diffusion weighting, using 2 averages, an echo time of 106 ms and a repetition time of 7 seconds. The images had a 240-mm field of view and consisted of 256 by 256 voxels.

For each study patient, the B0 and B1000 DWI images were uploaded to an image-processing workstation and converted to a 3-dimensional image format for analysis. The B1000 image was then scull stripped using the Brain Extraction Tool, which uses a model to fit the brain's surface.[16] This process is automated, robust, and extensively tested on a variety of MRI scanners and sequencers. Subsequent to this, FSL was used to segment images into gray matter, white matter, and cerebrospinal fluid.[17] Douaud et al first analyzed structural data with FMRIB Software Library-Voxel Based Morphometry, which performed brain extraction and bias field correction.[18] The brain volume for each patient was estimated by calculating the sum of all voxels in the gray and white matter volumes.

For each patient, the B1000 was used to identify the area of infarct and, using a 1-mm brush, the lowest slice of the diffusion restriction area was manually marked as a region of interest (ROI). The B0 image was then used to identify the MCA M1 stem in the highest slice on the ipsilateral side of the infarct. An ROI on the M1 stem was marked using a 1-mm brush along its length, if possible, until the junction of the distal bifurcation (Fig 1). To ensure standardization, 1 assessor (S.S.K.) marked the