

**Association between signal intensity gradient of cerebral arteries from time-of-flight
magnetic resonance angiography and clinical outcome in patients with lenticulostriate
infarction: A multicenter retrospective cohort study**

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Study population

This study is a multi-center, retrospective cohort study for all consecutive patients. From January 2015 to March 2021, patients who were diagnosed with acute ischemic stroke in the lenticulostriate artery (LSA) territory were registered at three centers (Jeonbuk National University Hospital, Samsung Medical Center, and Gunsan Medical Center). The 3 centers have their own characteristics: Gunsan Medical center is in a small city where about 300,000 citizens live, Jeonbuk National University Hospital is in a medium sized city where about 650,000 citizens live, and Samsung Medical Center is in a capital city where about 10,000,000 citizens live).

The inclusion criteria were as follows: (1) Patients aged 18 years or older who had brain magnetic resonance imaging (MRI) for acute ischemic stroke within 3 days, (2) Patients who underwent diffusion-weighted imaging (DWI) and apparent diffusion coefficient of the cerebral parenchyma, and cerebral angiographic measurements, in which, intracranial arteries should be examined by time-of-flight (TOF) techniques, and (3) A patient with high signal intensity lesions in the unilateral LSA territory on DWI.

The exclusion criteria are as follows. (1) Patients younger than 18 years of age, (2) Patients with moderate to severe ($>50\%$) stenosis or occlusion of the major intracranial and extracranial arteries, including internal carotid artery (ICA), middle cerebral artery (MCA), anterior cerebral artery (ACA), posterior cerebral artery (PCA), basilar artery (BA), and vertebral artery (VA), (3) Patients whose ischemic stroke was due to or related with cardiac or rare etiology (e.g., arterial dissection, moyamoya disease). The present study was conducted following approval from the ethics review committee in each hospital.

Acquisition of clinical data

Demographic and clinical information on cardiovascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, and smoking history), laboratory findings at admission (including complete blood count, lipid profiles, serum glucose level, HbA1c) were extracted from electronic medical records. A neurological severity in each patient was monitored using National Institute of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) during hospitalization, and were collected.

Clinical outcome

As a clinical outcome of the patients with the LSA infarction, mRS of discharge or 7th day was used to define clinical status: mRS 2 or less was defined as a good outcome group and 3 or more as a poor outcome group.

Time of Flight Magnetic Resonance Angiography

The MRA protocols in 3 hospital were described in detail, as in supplementary table 1. We used a 3.0T MR of a SENSE 32 Channel cardiac coil (Philips Medical Systems, Achieva, The Netherlands) to obtain a three-dimensional intracranial and extracranial TOF image. The parameters used to obtain TOF-MRA are as follows. TR = 23.0ms, TE = 3.5ms, Resolution = 300X220, FOV (field of view) = 180 mm², 160 slices, FA (flip angle) = 20.0°, scan duration = 1 minute 53 seconds – needs to be rewrite

Measurement of TOF MRA SIG from cerebral arteries

TOF MRA SIGs from cerebral arteries (both ICA, MCA, ACA, PCA, VA and one BA) were measured with a semi-automated software (VINT, Mediimage, Inc. Seoul, Republic of

Korea), as reported previously.¹ In brief, the signal intensities at the iso-point (Φ_a ; *signal intensity at position A [Xa] along the arterial contour line*) and at the inner point (Φ_b ; *signal intensity at position B [Xb]*) were calculated by using a trilinear interpolation algorithm based on the positions and signal intensities in the eight neighboring voxels. The signal intensities of TOF-MRA were normalized to eliminate the offset and scale effects across the MRA datasets of participants. For each iso-point (position A), the SIG was calculated from the difference in signal intensities between points A and B as follows:

$$\text{SIG, SI/mm} = (\Phi_b - \Phi_a) / |X_b - X_a| \quad (1)$$

The mean values of SIG of cerebral arteries were obtained, as shown in Figure 1. The arterial SIG measurement was performed in the straight segment as possible in ICA (at the C1 distal portion before a horizontal intrapetrous segment), VA (V4 distal, just before a conjoined BA), and BA (mid to distal portion). For the MCA and ACA, the initial 1/2 or 1/3 segment was chosen. For the PCA, P2 segment (distal to posterior communicating artery) was selected for a measurement.

Statistical analysis

Descriptive data for the clinical characteristics and laboratory findings of the participants were expressed as a mean \pm standard deviation or percentage as appropriate. Kolmogorov-Smirnov test was performed for distributional adequacy. A student t-test or chi-square test was used to assess differences as appropriate. Logistic regression analyses were performed to determine the independent association between the SIG values in cerebral arteries and favorable outcome, adjusting for all possible confounders. Statistical analyses were conducted using SPSS version 20 (SPSS, Chicago, IL, USA).

