Intracranial Arterial Calcification Can Predict Early Vascular Events after Acute Ischemic Stroke

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Background: Intracranial arterial calcification (IAC) is an evidence of advanced atherosclerosis. This study was aimed to investigate whether IAC predicts early vascular events (EVEs) during acute period of ischemic stroke. *Methods:* We prospectively enrolled consecutive patients with acute ischemic stroke and transient ischemic attack within 48 hours from January 2005 to October 2012. Three IAC categories were defined according to the total IAC score as follows: no IAC (0 point), mild IAC (1-2 points), and severe IAC (≥3 points). EVEs included early progression/recurrence of stroke, coronary events, and vascular deaths within 2 weeks from stroke onset. We used multivariable Cox regression analyses to determine the effect of IAC on EVE. *Results:* In the trend analysis of 1017 total patients, there were significant trends of increased IAC toward higher total EVEs (10.5% versus 13.8% versus 21.2%, $P < .001$). Severe IAC was related to increased rate of early progression/recurrence (hazard ratio [HR] 2.00; 95% confidence interval [CI] 1.07-3.71, $P = .029$) and coronary events (HR 3.51; 95% CI 1.00-12.31, $P = .050$) but did not show an association for mortality (HR .54; 95% CI .19-1.53, $P = .224$). Increased IAC was also related to a poor functional outcome after 3 months (odds ratio 2.23; 95% CI 1.38-3.59). *Conclusions:* IAC was significantly associated with increased early progression/recurrence of stroke and coronary events during acute period of ischemic stroke. IAC on the initial brain computed tomography would be used as a predictor for recurrent vascular events after acute ischemic stroke before further angiographic evaluation. **Key Words:** Vascular calcification—acute ischemic stroke—recurrent stroke—cerebral arteries.

Introduction

Arterial calcification or calcified plaque is related with advanced atherosclerosis.[1] Coronary arterial calcification is a strong and independent predictor of coronary heart disease,[2] cardiovascular event, and stroke.[3,4] Extracranial carotid arterial calcification is common in patients with cerebral ischemia and associated with severe luminal stenosis.[5] Arterial calcifications in major blood vessels including coronary, aortic arch, and carotid arteries are associated with volume of white matter ischemic lesion and cerebral infarction.[6] Intracranial arterial calcification (IAC) is commonly noted on brain computed tomography (CT) scans in 40%-80% of ischemic stroke patients.[7-9] It is associated with mortality and vascular events in ischemic stroke patients after hospital discharge.[9]

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Early vascular events (EVEs) including progression/recurrence of stroke, coronary events, and cardiovascular death are associated with large size infarction,[10,11] stroke severity,[12] and vascular status.[13,14] However, we hardly know the severity of infarction and the degree of vascular stenosis until taking brain magnetic resonance (MR) image and angiography that are not routinely conducted in the emergency room.

Although IAC can be frequently observed by initial brain CT in acute stroke, no study has been reported on the relationship with EVEs. The aim of this study was to determine whether increased IAC predicts EVEs during acute period of ischemic stroke.

Methods

Study Population

Our study prospectively enrolled consecutive patients with acute ischemic stroke or transient ischemic attack (TIA) within 48 hours from onset in the stroke registry of Soonchunhyang University Hospital between January 2005 and October 2012 (n = 1236). Excluding an absence or poor quality of brain CT scan (n = 182) and insufficient data or records (n = 37), this study finally included 1017 subjects with ischemic stroke (939, 92.3%) and TIA (78, 7.67%). This study was approved by the local institutional review board.

Measurement and Grading of IAC

Brain CT scans were performed by a 64-channel multidetector CT scanner (Somatom Sensation 64; Siemens, Berlin, Germany). All brain CT studies were performed with a same 5-mm slice thickness from the skull base to the vertex. Arterial calcifications were defined as hyperdense foci with a peak density more than 90 Hounsfield units. IAC degree was categorized according to calcification along the circumference in the densest calcified segment of each vessel. IAC score was categorized as 0 point (no calcification in any of the CT slices), 1 point (mild calcification, calcification <50% of circumference), and 2 points (severe calcification, ≥50% of circumference)[8] (Fig 1).

The total IAC score ranged from 0 to 12 (up to 2 points per the most calcified area of both internal carotid arteries, anterior cerebral arteries, middle cerebral arteries, posterior cerebral arteries, vertebral arteries, and basilar artery). Three IAC categories were defined according to the total IAC score as follows: no IAC (0 point), mild IAC (1-2 points), and severe IAC (≥3 points).[8] IAC scores were rated with an axial image of initial brain CT by 2 neurologists (L.J.G. and L.K.B.), blinded to the medical information and clinical outcomes. Inter-rater reliability was assessed with the Cohen kappa statistics (κ = .856).

Outcome Catchment

The subjects were prospectively observed for EVE during the first 2 weeks of acute period. EVE included early progression or recurrence after primary ischemic stroke, coronary event, and vascular death. Early progression was defined as a neurologic worsening by 2 or more point increases of the NIHSS score within 24 hours from onset after stabilization of neurologic deficit. Those beyond 24 hours from onset were defined as early recurrence.[15,16] NIHSS measuring were performed at 24 hours, on day 7 and day 14, and at discharge. All events were confirmed by follow-up diffusion-weighted MR imaging or brain CT by another neurologist (R.H. and A.M.Y.) who were blinded to the IAC score. Neurologic deteriorations because of hemorrhagic transformation or herniation were excluded. Coronary events were defined as one of the following: acute coronary syndrome containing unstable angina and myocardial infarction during hospitalization based on clinical symptom, change of electrocardiogram, and cardiac biomarker (troponin I, troponin T, or creatine kinase-MB).[17,18] Vascular death was defined as fatal stroke (death because of brain edema or herniation), fatal myocardial infarction, or sudden death that was not attributed to any other causes. More than 3

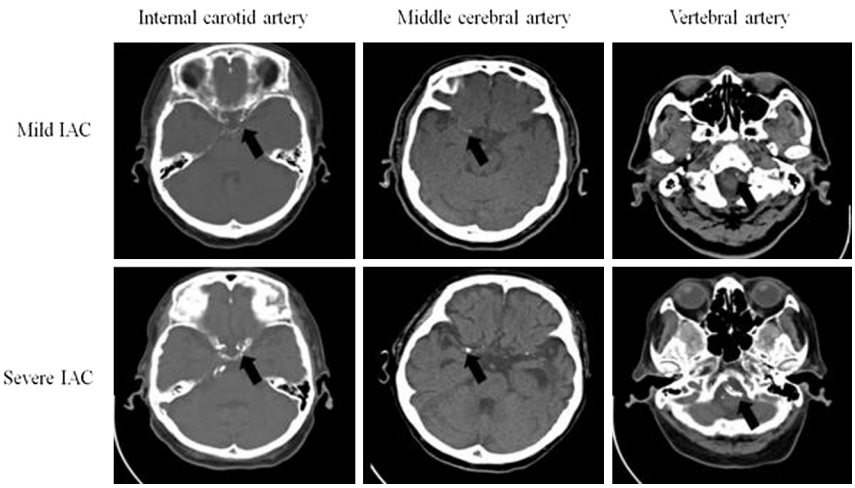

Figure 1. *The degree of IAC in major intracranial vessels. Abbreviation: IAC, intracranial arterial calcification.*