### The Application of Ultrasonic Velocity Vector Imaging Technique of Carotid Plaque in Predicting Large-Artery Atherosclerotic Stroke

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Background: Large-artery atherosclerotic stroke (LAAs) is related to carotid plaque, but the mechanical mechanism is unclear. We aimed to use ultrasonic velocity vector imaging (VVI) technique to study the mechanical difference of carotid plaque in patients with LAAs and controls. Methods: We enrolled 43 LAAs patients and 38 controls but all showing plaque on carotid ultrasonography. Ultrasonic VVI technique was used to analyze radial systolic and diastolic peak velocity (R-vs, R-vd), radial and circumferential peak strain (R-s, C-s) and radial displacement (R-dis) of carotid plaque. Results: Compared with controls, LAAs patients showed higher pulse pressure (P = .001), pulse pressure index (PPI, P = .006), and greater stress at carotid plaque as manifested by higher absolute value of radial diastolic peak velocity (R-vd, P = .021), radial systolic peak velocity (R-vs, P = .007), radial peak strain (R-s, P = .015), and radial displacement (R-dis, P = .022). PPI was significantly correlated with R-vs (r = -.274, P = .013), R-vd (r = .304, P = .006), and R-dis (r = -.28, P = .011). But there was no correlation between R-s and blood pressure. R-s was screened to be the most predictable parameters for LAAs (odds ratio, 1.118; 95% confidence interval, 1.012 $\sim$ 1.236; P = .029). The area under the curve of R-s was .627. Conclusions: Radial peak strain (R-s) is a predictable parameter for the occurrence of LAAs. We predict using ultrasonic VVI technique to analyze whether the mechanics of carotid plaque is helpful to screen patients with high risks of LAAs. Key Words: Carotid plaque—velocity vector image technique—strain large-artery atherosclerotic stroke.

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Atherosclerotic plaque vulnerability is the major pathogenesis of coronary heart disease and large-artery atherosclerotic stroke (LAAs), both with high morbidity and mortality worldwide. Vulnerable plaque is commonly defined as plaque with thin fibrous cap, lipidrich core, infiltration of abundant inflammatory cells,

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This work was supported by The National Basic Research Program of China (973 Program, 2011CB503906, 2010CB732605), the HI-TECH neovascularization, spotty calcification, and positive vascular remodeling, according to pathology research involving humans and animal model. Besides those intrinsic properties, plaque vulnerability is also associated with mechanical stress, which is affected by plaque composition, anatomy, shape, and external circumstances

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including blood components and hemodynamic characteristics.<sup>1,2</sup>

Carotid ultrasonography has been widely used to screen patients at high risk of cerebrovascular disease because carotid plaques are markers of generalized atherosclerosis and sources of thromboemboli for LAAs.3-5 Ultrasonic velocity vector imaging (VVI) is a relatively new and reliable tool that could be used for analyzing the regional mechanics of local tissue in terms of strain, strain rate, and displacement. In recent years, this technique has been increasingly used in mechanical research of blood vessels.<sup>6-10</sup> And researchers have found that there was significant correlation between VVI indexes and histologic property.<sup>11,12</sup> LAAs is related to carotid plaque, but the mechanical mechanism is still unclear. We aimed to use ultrasonic VVI technique to study the mechanical differences of carotid plaque between patients with LAAs and controls without cerebrovascular history.

### Methods

#### Study Group

Consecutive patients referred to our department for echocardiography from September to December in 2010 were screened by medical history and carotid artery ultrasonography. Inclusion criteria for LAAs group was that patients were hospitalized in the neurology department with the presence of carotid plaque and a final diagnosis of LAAs according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST)<sup>13</sup> classification by checking neurologic signs, symptoms, and cranial magnetic resonance imaging. And the stroke was new onset within 2 weeks. We excluded patients with any history of atrial fibrillation, rheumatoid heart disease or valve replacement, lacunar stroke, or embolic stroke with a definite cause. The controls were also in-patients who came to our department for ultrasound examination showing carotid plaque in the same period but with no cerebrovascular disease according to medical history and physical examination.

#### Medical History and Traditional Risk Factors

General information of age, sex, and medical history, including data of hypertension, diabetes mellitus, cerebrovascular disease, present history, and chief complaint, were obtained by questionnaire. Experienced neurologists performed physical examination. Blood pressure (BP) was measured manually at right brachial artery around the upper arm 1 inch above the elbow joint<sup>14</sup> after ultrasonic examination. Pulse pressure (PP) was calculated as systolic blood pressure (SBP) minus diastolic blood pressure (DBP; SBP – DBP). Pulse pressure index (PPI) defined as PP/SBP reflects vascular compliance.<sup>15</sup> Fasting blood samples were taken, and creatinine, fasting glucose, low-density lipoprotein, and high-density lipoprotein were measured.

#### Transthoracic Echocardiography

All subjects underwent transthoracic echocardiography. The Simpson's method was used for measuring left ventricular ejection fraction (LVEF) at apical windows.

#### Carotid Artery Ultrasonography

Acuson Sequoia 512 ultrasound system (Siemens Medical Systems, Mountain View, CA) with 15L-8 probe ( $10\sim14$  MHz) was used for bilateral carotid artery examination. The presence of plaque was defined as a focal lesion of at least .5 mm that encroached into the arterial lumen or demonstrated a thickness of 1.5 mm as measured from the media-adventitia interface to the intima-lumen interface.<sup>16</sup> The thickness of carotid plaque, intima-media thickness, and the radius of carotid artery were measured.

With ultrasonography under the VVI mode, we amplified the region of interest. A single-beat dynamic image of both longitudinal and transverse plane of the carotid plaque at the thickest part was stored for off-line analysis.

Syngo US VVI software was used to analyze the mechanical characteristics of carotid plaque. For transverse images, we chose the "short axis" mode and manually traced 2 circles evenly around the media-adventitia interface and intimae-lumen interface, respectively. The software tracks the tissue movements automatically. The circles were divided into 6 equal segments. The radial diastolic peak velocity (R-vd) and radial systolic peak velocity (R-vs), the radial peak strain (R-s) and circumferential peak strain, and the radial peak displacement (R-dis) curves of the 6 segments were displayed (Fig 1). The numerical value of radial peak velocity (R-vd and R-vs), R-s and circumferential peak strain, and R-dis of the plaque part were recorded. Because the reference point is placed in the center of carotid artery and the carotid expands far away from the center in cardiac systolic period, the value of radial strain and displacement and systolic velocity is negative, whereas the value of the radial diastolic velocity is positive. All indexes used the absolute value for discussion to facilitate understanding.

#### Data Analysis

Statistical analysis involved use of SPSS v18.0 (SPSS Inc., Chicago, IL). Data are expressed as mean  $\pm$  standard deviation. Unpaired *t* test was used to compare differences in quantitative variables. We used Pearson coefficient correlation to explore the relationship between different indexes. Binary logistic regression was used to derive predictors of LAAs. Receiver operating characteristic curve (ROC) analysis was used to estimate the predictive value of the significant risk factors for LAAs. *P* less than .05 was considered statistically significant.

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