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● *Original Contribution*

SEVERITY OF SPONTANEOUS ECHO CONTRAST IN THE JUGULAR VEIN ASSOCIATED WITH ISCHEMIC STROKE

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Abstract—This study evaluated the relationship between spontaneous echo contrast (SEC) in the internal jugular vein (JV), atherosclerotic markers and ischemic stroke. One hundred twenty patients with acute ischemic stroke and 120 controls were recruited. SEC score correlated with plasma level of fibrinogen (coefficient: 0.105, $p = 0.022$), hemoglobin (coefficient: 0.122, $p = 0.008$) and presence of JV reflux (coefficient: 0.314, $p < 0.001$) and peak flow velocity (coefficient: −0.244, $p < 0.001$) in the corresponding JV, but did not correlate with carotid plaque score (coefficient: 0.042, $p = 0.358$) or intima-media thickness (coefficient: 0.067, $p = 0.303$). Multivariate regression analysis revealed that fibrinogen level, SEC score, intima-media thickness, plaque score and history of coronary artery disease were associated with acute ischemic stroke. In conclusion, the severity of SEC in the JV might represent the tendency toward thrombogenesis in diseased cerebral circulation possibly through mechanisms other than arterial atherosclerosis. (E-mail: Hungyihsu@gmail.com) © 2014 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Carotid artery, Ischemic stroke, Jugular vein, Spontaneous echo contrast, Ultrasonography.**

INTRODUCTION

Spontaneous echo contrast (SEC) is a peculiar ultrasonographic finding characterized by a swirling, smoke-like echo of blood flow that can be observed in heart chambers, aneurysms, large arteries and veins. Regions characterized by low flow and low shear rate have been correlated with increased formation of SEC (Fatkin et al. 1994b; Merino et al. 1992). Plasma proteins, red blood cells, white cells and platelets have also been reported to be involved in the formation of SEC (Fatkin et al. 1997; Merino et al. 1992; Rastegar et al. 2003). SEC in various parts of the circulatory system could have similar clinical and prognostic significance. SEC in both left atrium and aorta was associated with systemic embolization and cardiovascular diseases including stroke (Chimowitz et al. 1993; Daniel et al. 1988; ELAT Study 1995; Fatkin et al. 1994a; Pitsavos et al. 2003). SEC in the internal jugular vein (JV) can be examined easily, but has usually being overlooked. Our previous study found that the severity of SEC in the JV could be an indicator of a systemic prothrombotic state (Hsu et al. 2012). Furthermore, SEC in the JV was reported to occur more frequently in patients with previous ischemic stroke (Hsu et al. 2012). However, the relationship between SEC in the JV and atherosclerosis is unknown. Previous studies found a close link between venous and arterial thromboembolism. Venous and arterial thromboembolism share the same risk factors (Anderson et al. 1991; Cogo et al. 1994; Libertiny and Hands 1999). Some anti-thrombotic agents and statins, which help to prevent cardiovascular events, also reduce the risk of venous thromboembolism (Fatkin et al. 1994b; Grady et al. 2000; Ray and Rosendaal 2001; Ray et al. 2001). The usefulness of SEC in the JV as a surrogate marker of cerebral vascular disease or a target of treatment requires further study. This study was

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conducted to evaluate the relationship between the severity of SEC in the JV and acute ischemic stroke (AIS) and to evaluate the association between SEC in the JV and markers of atherosclerosis.

METHODS

Patients

Consecutive patients who were admitted to Taichung Veterans General Hospital for AIS within 7 d of stroke onset were screened by experienced neurologists prospectively. All stroke patients fulfilled the World Health Organization criteria of stroke and had no evidence of hemorrhage on their cranial imaging studies. Patients were excluded if they had cardiopulmonary distress, significant cardiac arrhythmia or difficulty in performing respiratory maneuvers during ultrasound examination. All stroke patients received routine workups for a stroke risk factor and etiology survey. All blood tests and ultrasonographic examinations were performed within 3 d after admission. The National Institutes of Health Stroke Scale (NIHSS) was used to evaluate the severity of a stroke. All strokes were classified into five major subtypes according to the Trial of ORG 10172 in Acute Stroke Treatment criteria (Valdueza et al. 2013). In total, 120 stroke patients were recruited. For comparison, an additional 120 patients who had no previous history of cerebrovascular disease were recruited as controls from a group of individuals who received health checkups including carotid duplex ultrasonography in this hospital. This study was approved by the institutional review board of this hospital. All participants signed informed consent before entering the study.

Past medical history and risk factors for atherosclerosis were recorded on a standard form for all recruited patients. Fasting blood samples were obtained from all participants. All patients received blood tests including complete blood cell counts, biochemical analyses, coagulation studies and plasma levels of fibrinogen and high-sensitivity C-reactive protein (hs-CRP).

Ultrasonography of carotid arteries and internal jugular veins

A computed ultrasound system (Sonos 5500, Hewlett Packard, Andover, MA, USA) equipped with a linear multifrequency 3.0- to 11.0-MHz probe was used for both carotid artery and JV examination. The same experienced sonographer performed all ultrasonography. Carotid arteries were examined in the supine position by standard procedures (American Institute of Ultrasound in Medicine 2003). For measuring carotid plaque score, the carotid artery was divided into five segments: proximal common carotid artery, distal common carotid artery, carotid bifurcation, internal carotid artery and external carotid artery (Hsu et al. 2002). All arterial segments underwent longitudinal and transverse scanning to evaluate the characteristics of atherosclerotic plaque. The percentage of vessel obstruction of each arterial segment was measured along the longitudinal axis and classified as local diameter stenosis $\leq$30%, 31%–50% or $>$50%. When multiple plaques were found in any segment, the greatest degree of obstruction was recorded, as were the number and site of associated smaller lesions. Carotid plaque score was calculated based on the severity of plaque in each segment using a method described elsewhere (Hsu et al. 2002; Sutton-Tyrrell et al. 1992). Plaque and carotid intima-media thickness (IMT) were defined by the criteria suggested by the Mannheim consensus (Touboul et al. 2012). The IMT of the common carotid artery was obtained and expressed in millimeters. The maximal thickness of the far-wall intima-media layer within 1 cm proximally to the carotid bifurcation was obtained manually at the bilateral common carotid arteries; the average of bilateral carotid IMTs was used for statistical analysis.

All participants were in the supine position with their heads in a neutral position during JV examination. Great care was taken to prevent external compression of the internal jugular veins with the ultrasound probe. The highest B-mode gain that did not produce artificial echoes was used to acquire B-mode images for SEC analysis. The B-mode images had a dynamic range of 64 dB. Ultrasound loops of JV were acquired during resting, breath holding and brief Valsalva maneuver. All ultrasound studies were stored digitally for later analysis. The details of jugular vein ultrasonography and the criteria of JV reflux are described elsewhere (Hsu et al. 2008). The severity of SEC in each JV was quantified by using a scoring system developed in our laboratory. SEC was recognized on ultrasound images by the characteristic flowing and swirling echoes in the JV (Supplemental Videos 1 and 2). SEC in the JV was quantified with a custom-designed grading system based on the density of SEC (Fig. 1) and the percentage of JV lumen occupied by SEC (Hsu et al. 2012). The carotid plaque score and SEC score were graded offline by the same experienced neurosonologist who was unaware of the participants' clinical information. The total SEC score, which was the sum of bilateral SEC scores in each individual, was used for statistical analysis.

Statistical analysis

Continuous variables are expressed as means $\pm$ standard deviations. Categorical variables are expressed as numbers and percentages. The non-parametric Mann-Whitney test was used to compare differences between control patients and stroke patients. The Kruskal-Wallis test was used to compare differences among different