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● *Original Contribution*

COMPARISON BETWEEN QUANTITATIVE STIFFNESS MEASUREMENTS AND ULTRASONOGRAPHIC FINDINGS OF FRESH CAROTID PLAQUES

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Abstract—Using a stiffness meter, we quantitatively measured the stiffness of fresh plaques that had been excised by carotid endarterectomy. The objective of this study was to clarify the correlation between plaque stiffness and pre-operative carotid ultrasonographic findings, and predict the stiffness of plaques before surgery by comparison with the stiffness of common items. The study population comprised 44 patients (44 lesions) who had undergone carotid endarterectomy at our institution between December 2009 and October 2014. The stiffness of excised fresh plaques was measured using a stiffness meter and compared with the pre-operative echographic findings for the plaques and the stiffness of selected foods and common items. The mean stiffness value for all plaques was 4.52 ± 3.30 MPa (mean ± standard deviation). The plaques exhibiting calcification were significantly harder (p = 0.001). On classification of lesions on the basis of echographic findings, plaque hardness was in the order low-echoic (15 lesions) < iso-echoic (20 lesions) < high-echoic (9 lesions) (p = 0.02). The stiffness of the low-echoic group was equivalent to that of tofu or sliced cheese, whereas the plaques in the iso- and high-echoic groups exhibited stiffness similar to that of ham and a plastic eraser, respectively. A significant correlation was observed between the quantitative stiffness values of carotid plaques and their brightness on carotid ultrasonography. Using these data, operators might be able to predict plaque stiffness from pre-operative echographic findings. In addition, it might be useful for operators to compare such quantitative stiffness measurements with stiffness data for foods and common items to gain an understanding of the state of the target plaque before treatment. (E-mail: k-kondo@med.toho-u.ac.jp)   © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Carotid plaque, Ultrasonography, Plaque stiffness, Carotid endarterectomy, Stiffness meter.**

INTRODUCTION

Carotid artery stenosis is caused by arteriosclerotic changes in the cervical carotid bifurcation. It was previously considered to develop more frequently in Westerners, but its incidence in Japan has increased with changes in diet, lifestyle and aging (Iwasaki et al. 2008). An arteriosclerosis-induced localized intimal protrusion exceeding 1 mm is termed a *plaque*. The thickening of such plaques leads to carotid artery stenosis, which can cause cerebral infarction (Cao et al. 2003; Davies 2000; Inoue et al. 2007; Nowaczenko et al. 2003; O'Leary et al. 1999).

Cerebral infarctions develop from carotid artery stenosis *via* two main pathogenic pathways: hemodynamic development caused by the progression of stenosis and embolisms caused by plaque dispersion (Molloy and Markus 1999; Verhoeven et al. 2005). In the former, the risk of cerebral infarction can be reduced by resolving stenosis, and the surgical indication is decided based on the degree of stenosis and the presence or absence of other neurologic symptoms (Barnett et al. 1998; European Carotid Surgery Trialists' Collaborative Group 1995, 1998; Executive Committee for the Asymptomatic Carotid Atherosclerosis Study 1995; Hobson et al. 1993; Mayberg et al. 1991; North American Symptomatic Carotid Endarterectomy Trial Collaborators 1991; Rothwell et al. 1994). For the latter, plaques with various properties likely to serve as a source of embolism have been reported, but evidence

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is still insufficient. Thus, the conditions for surgical indication based on plaque properties have not yet been established (Aburahma et al. 2002; Grønholdt et al. 2001; Rothwell et al. 1994; Yuan et al. 2002).

Carotid ultrasonography is a non-invasive, simple test that is generally used to examine carotid artery stenosis. In addition to being useful for measuring the rate of stenosis, it is superior in evaluating plaque properties. Echo findings of plaques likely to become a source of embolism include low echogenicity, heterogeneity, ulceration and irregular surface (Elatrozy et al. 1998; Lee 2014). Of these, high consistency of the brightness with histopathologic findings is known (Czernuszewicz et al. 2015). Close involvement of soft plaque in the development of embolic infarction has been pointed out, and the subjective evaluation of plaque stiffness has occasionally been reported (Lee et al. 1992; Ohayon et al. 2008; Williamson et al. 2003).

Carotid stenosis is treated mainly by carotid endarterectomy (CEA) and carotid artery stenting (CAS). CEA is a surgical treatment in which the intima–media complex (IMC) of the stenotic region is excised (Javid and Tylon 1978). CAS is an interventional therapy in which the stenotic region is dilated by inserting a metal stent (Diethrich et al. 1996; Ederle et al. 2007). Although it is a newer method than CEA, performing CAS with a protective device to prevent distal embolisms has been found to be comparably effective and tolerable compared with CEA in high-risk patients (Gurm et al. 2008; Yadav et al. 2004).

In the study described here, we used a stiffness meter to quantitatively measure the stiffness of fresh plaques that had been excised by CEA. For this method of measuring the carotid intima, past literature is helpful in measuring the mechanical properties (Maher et al. 2009; Stemper et al. 2005). The objective of this study was to clarify the correlation between the quantitative stiffness values of plaques and their pre-operative echographic findings, and to obtain data that could be used to predict plaque stiffness before treatment. In addition, the stiffness of the plaques was compared with those of selected foods and common items to provide operators with easy-to-understand examples of stiffness.

METHODS

Study sample and data collection

This study was approved by the ethics committee of Toho University (Approval No. 2500622035). Written informed consent was obtained from all patients for CEA.

Patient population

Of 47 consecutive patients treated with CEA at our institution between December 2009 and October 2014, comparisons of plaque stiffness with pre-operative carotid ultrasonography findings were possible in 44 patients (44 lesions), who were subsequently selected for participation in this study (including 41 males, mean age: 69.7 ± 7.4 y).

Carotid ultrasonography

A XARIO SSA-660 A (Toshiba Medical Systems, Tochigi, Japan) was used as the measurement device, and a PLT-805 AT (Toshiba Medical Systems, Tochigi, Japan) and a PLT-704 AT (Toshiba Medical Systems, Tochigi, Japan) were used as transducers. The frequency of the transducer was 8.0 MHz. During each examination, the neck of the subject, who was in the supine position, was extended to widen the observation field, and the head was tilted toward the healthy side. Tomographic images of the carotid artery were obtained along the minor and major vascular axes. Supplementary cans of difficult-to-visualize regions were obtained in two or more anterior and lateral directions, and the common carotid artery, carotid bulb and internal carotid artery were specified as essential observation regions. To evaluate the plaques, intima–media thickness (IMT) of the thickest part of the plaque, that is, the maximum IMT (max IMT), was measured on tomographic images obtained in the systolic phase of the artery. From these measurements, diameter- and area-based degrees of stenosis of the target artery were determined using the European Carotid Surgery Trial (ECST) and area methods, respectively (European Carotid Surgery Trialists' Collaborative Group 1991). The presence or absence of ulceration of the plaque surface was also evaluated. In addition, the brightness of the narrowest region of the plaque was classified as low-echoic, iso-echoic or high-echoic based on the brightness of the IMC near the plaque. Plaques that were difficult to classify were assigned to the mixed type, and when the brightness of a plaque's internal echo signals could not be determined because of calcification, it was regarded as indistinguishable.

Quantitative stiffness measurement with a stiffness meter

A CR-500 DX-S II rheometer (Sun Scientific, Tokyo, Japan) was used as the stiffness meter (Fig. 1a). Stiffness was measured by pressing the sample on a measurement table with a special adaptor (Fig. 1b). Rheo Data Analyzer VR.2.8 g3 (Sun Scientific, Tokyo, Japan) was used as analytical software, and stiffness values are presented in megapascals (MPa). Tofu, sliced cheese, ham, a plastic eraser and a stick of gum were selected as reference materials as they are common and recognizable items, and their stiffness is easy to imagine. These materials were cut into 1 × 1-cm pieces, and the