REAL TIME ELASTOGRAPHY ASSESSMENT OF THE STIFFNESS OF CAROTID PLAQUES: INITIAL CLINICAL EXPERIENCE

YAN TIAN,*, XUEQIANG FAN,*, JIAOHAO MA, JINGPING WU, CHENGLONG ZHENG, JIAN LIU, YAN HUANG, LIN YANG, DANDAN GUO, JIECHEN, XIA ZHENG, XUENI SONG, HAIYANG ZHANG, MIN ZHENG

1Department of Ultrasound Diagnosis, China-Japan Friendship Hospital, Beijing, China - 2Department of cardiovascular surgery, China-Japan Friendship Hospital, Beijing, China - 3Department of Traditional Chinese medicine, The Gulou Hospital of TCM, Beijing, China

* Both Authors contributed equally to this research.

Introduction

Carotid atherosclerosis is an important health problem with a high burden of disease in the western world and in developing countries, 88% of patients with amaurosis fugax or hemispheric transient ischemic attacks have atherosclerotic disease at the carotid artery[1]. It is important to early diagnose and manage in carotid atherosclerosis with the aim of controlling adverse cerebral and cardiovascular events[2]. Several noninvasive techniques evaluated for the characterization of the plaque may have implications for treatment[3]. With the advent of vascular ultrasound in the 1980s, it became possible to identify arteriosclerosis in the carotid artery noninvasively. Real time elastography (RTE) is a newly developing technique that can reflect the tissue stiffness by measuring the degree of tissue’s deformation. This technique has previously been shown to be useful in the differential diagnosis between benign and malignant tumors[4], but few assess the stiffness of carotid plaque. In this study, the stiffness of carotid plaques with RTE was assessed.

Materials and methods

The Research Ethics Committee of our hospital approved the prospective study protocol, and informed consents were obtained before their ultrasound elastography examination.

Patients

From January 2012 to April 2014, 96 patients enrolled. (28 women and 68 men; mean age, 63.61
±10.61 years; range, 35-91 years). The inclusion criterion was the presence of single or multiple posterior carotid wall plaques, thickness of plaque ≥ 2mm.

**Equipment**

All the patients were examined using a Hitachi VISION Preirus System machine (Hitachi Medical Corporation, Tokyo, Japan) with 5-13 MHz broadband linear array transducer. For real-time elastography, the system employs quantitative software (combined autocorrelation method, provided by Hitachi Medical).

**Ultrasound techniques**

Ultrasound examinations were performed by the same sonographer with more than 5 years’ experience of carotid artery ultrasound. For each enrolled carotid plaque, ultrasound features including position, shape, size, surface and calcification were evaluated.

**RTE examination**

After conventional ultrasound examination, the RTE examination was performed on each plaque. The entire RTE examination lasted average 8-10 minutes per patient. All the RTE examinations were performed by the same sonographer with experience of more than 50 cases of carotid artery RTE.

Higher levels of pressure can manifest nonlinear properties of tissue elasticity. Satisfactory elastic image criteria are as follows:

1) The image is clear and stable, and the image is maintained at 2-3s;
2) RGB (Red-Green-Blue) signs of carotid artery plaque in region of interest (ROI);
3) ROI is completely covered by color encoding.

Elastography imaging was obtained on longitudinal planes. The ROI was usually two times of the lesion including sufficient surrounding vessel wall and muscle. The acquired echo signals were used to calculate tissue strain with the combined auto-correlation method. RTE software displays elastogram using a scale from red (highest strain; soft), through green to blue. The elastogram image and B-mode image were displayed simultaneously in dual mode. Meanwhile, RTE was used to calculate the ratio of the stiffness of carotid plaque. To minimize transient temporal fluctuations, 3 optimal static image and 3 groups of characteristic parameters will be stored for quantitative analysis.

**Statistical analysis**

Statistical analyses were carried out using Statistical Product and Service Solutions (Chicago, IL, USA) version 20.0. All quantitative data are expressed as mean±standard deviation. Comparison of categorical variables was performed using ANOVA. P<0.05 was considered to represent a statistically significant difference.

**Results**

**General features**

96 patients were included in our group (19 men, 20 women; mean age, 54.5±16.8 years, range 19-82 years). There was no difference between groups as for the patients’ age between different groups (p>0.05) (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypo-echo</td>
<td>58</td>
<td>62.10±10.44</td>
</tr>
<tr>
<td>Complex-echo</td>
<td>30</td>
<td>63.76±11.81</td>
</tr>
<tr>
<td>Strong-echo</td>
<td>21</td>
<td>67.38±8.49</td>
</tr>
</tbody>
</table>

Table 1: Demographic characteristics of the patients.

**RTE results**

The elastogram image and B-mode image of carotid plaque are shown in Figure 1. The hypo-echo regions in B-mode were consistent with the red or green regions in the real-time ultrasound elastogram, the complex-echo plaque display the green or blue regions in the elastogram; the strong-echo plaque display in the elastogram. Qualitatively, 58 of the 109 plaques were classified as hypo-echo, 30 were classified as complex-echo, and 21 were classified as strong-echo. The mean value of the strain ratio of hypo-echo carotid plaques is 1.21±0.69, the mean value of the strain ratio of complex-echo carotid plaques is 4.35±3.19, the mean value of the strain ratio of strong-echo carotid plaques is 41.14±33.09, and there was significant difference between them (p<0.05) (Table 2).

**Pathology results**

Future studies for detection of vulnerable carotid plaques include matching RTE images for patients scheduled for CEA surgery with plaque histology when it is subsequently removed. The image compared to the ‘gold standard’ of tissue specimens (Fig. 2).
It has been found that the occurrence of cerebral vascular events is not only related to the stenosis of the vessels\(^5\), but also the stability of plaque. The recognition of vulnerable plaque is also paramount in the surgical management of carotid atherosclerosis, particularly when CAS is planned\(^6\).

Plaque morphology includes surface and structure characteristics\(^7\). Carotid plaques with a large lipid core and thin fibrous cap are more likely to rupture\(^8\). Positron emission tomography (PET)-computed tomography (CT) and high-resolution magnetic resonance imaging (MRI), and multislice CT were proposed to evaluate plaque composition and inflammation\(^9\).

But they are high cost, radiation and not popularized equipment\(^10\). Ultrasound is widely used in clinical screening of carotid atherosclerotic lesions because of its low cost and the popularization of inspection equipment, but the traditional ultrasound examination has limited the ability to display the internal tissue components of the plaque\(^11\).

RTE is a newly developing technique that can reflect the stiffness of organs. Many experiments indicate that elastic differences in tissue can be sensitively detected by RTE\(^12\).

This study defined that the ultrasound plaque stiffness was found to have potential clinical value for improving the identification of the vulnerable carotid plaque. Under equal stress, the strain of the soft lipid plaques is greater than that of hard fiber plaques, because the mechanical properties of the fibrous plaques and lipid plaque components are different, and elastic imaging is likely to differentiate between different plaque components. Plaque elasticity imaging is a study of the deformation caused by the change of the plaque. The RTE image is needed to be a suitable pressure method. The routine use of the surface pressure method is not recommended for carotid artery plaque elasticity, because the changes of the blood pressure in the cardiac cycle. External pressure and blood pressure of cardiac cycle changes are difficult to achieve

**Table 2**: Significant difference of strain ratio between groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Strain ratio</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypo-echo</td>
<td>58</td>
<td>1.21±0.69</td>
<td>61.489</td>
<td>0.000</td>
</tr>
<tr>
<td>Complex-echo</td>
<td>30</td>
<td>4.35±3.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strong-echo</td>
<td>21</td>
<td>41.14±33.09</td>
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**Figure 1**: Color-coded RTE image and the B-mode image.

**A**: shows the matched B-mode and RTE images from the left common carotid artery of a 66-year-old male. The plaque is visible on the distal wall. The B-mode image indicates a bright border with a hypoechoic core. RTE imaging reveals a soft region (red image).

**B**: shows the matched B-mode and RTE images from the left bifurcate carotid artery of a 56-year-old male. The B-mode image indicates a hypoechoic plaque. RTE imaging reveals a soft region (green image).

**C**: shows the matched B-mode and RTE images from the right internal carotid artery of a 65-year-old male. The B-mode image indicates complex-echo image. RTE imaging reveals heterogeneous composition of stiffness.

**D**: shows the matched B-mode and RTE images from the right bifurcate carotid artery of a 75-year-old male. The B-mode image indicates strong-echo image.

**Figure 2**: Color-coded RTE image, the B-mode image and Corresponding pathological images.

**A-1**, The RTE image is blue. **A-2**, in histopathology, the lesion was the fibrous plaque, HE stain, 20×

**B-1**, The RTE image is mainly green. **B-2**, in histopathology; the lesion was the Atherosclerotic lipid plaque Plaque, HE stain, 20×

**C-1,C-2**: In the plaque calcification area RTE images showed a blue and white. Arrow indicates calcification

Discussion

It has been found that the occurrence of cerebral vascular events is not only related to the stenosis of the vessels\(^13\), but also the stability of plaque. The recognition of vulnerable plaque is also paramount in the surgical management of carotid atherosclerosis, particularly when CAS is planned\(^14\).

Plaque morphology includes surface and structure characteristics\(^7\). Carotid plaques with a large lipid core and thin fibrous cap are more likely to rupture\(^8\). Positron emission tomography (PET)-computed tomography (CT) and high-resolution magnetic resonance imaging (MRI), and multislice CT were proposed to evaluate plaque composition and inflammation\(^9\).

But they are high cost, radiation and not popularized equipment\(^10\). Ultrasound is widely used in clinical screening of carotid atherosclerotic lesions because of its low cost and the popularization of inspection equipment, but the traditional ultrasound examination has limited the ability to display the internal tissue components of the plaque\(^11\).
synchronization, plaque stress quantitative is difficult to master\textsuperscript{(13)}. Therefore, this study makes use of the changes in the blood pressure (systolic blood pressure and diastolic blood pressure) to make quantitative pressure changes more easily, through the pressure of the blood vessels themselves to form the pressure to carry out flexible imaging.

RTE showed that the hypo-echo plaques were mainly red or green, and complex -echo plaques were blue-green, and the strong-echo plaques were blue-white. In the examination of carotid artery plaque, the image includes muscle tissue, blood, and plaque (composition of lipid, fiber, calcification, bleeding, and the amorphous necrosis). The physical and mechanical properties of these tissues are different, so the deformation is also different under the influence of carotid artery pressure. Pathology results show that calcification display blue-white, fiber display blue and lipid, hemorrhage, necrosis display green or red. The color of the plaque in the study is consistent with the tissue pathology.

Elastic imaging strain ratio (A/B) indicates the relative value of the plaque and the neck muscle stiffness. The bigger A/B value indicate the harder carotid artery plaque, the smaller A/B value indicate the softer carotid artery plaque. This study showed that the strain ratio of the hypo-echo, mixed-echo and strong-echo carotid artery plaque increased in turn.

In conclusion, noninvasive RTE is a novel technique that characterizes plaque biomechanics by mapping carotid plaque strains (deformations)\textsuperscript{(14)}. It is low-cost, implementable on modern clinical ultrasound machines and could potentially accompany routine carotid imaging examinations\textsuperscript{(6)}. RTE can provide additional stiffness information to ultrasound operators and decrease equivocal diagnoses in the patients with cervical lymphadenopathy for unknown reason. This study of pathology results was based on small numbers, we need long-term studies to expand the sample size.

References


3) Matsuo Y, Takumi T, Mathew V, Chung WY, Barsness GW, Rihal CS, et al. Plaque characteristics and arteri


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Corresponding author

MIN ZHENG
Email: zhengmin16@163.com