Expansive arterial remodeling of carotid arteries in symptomatic ischemic patients

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ABSTRACT

Purpose: The present study aimed to assess the associations of expansive remodeling of carotid arteries with ischemic symptoms and the degree of stenosis.

Materials and Methods: A total of 41 symptomatic patients with vulnerable plaques and 25 asymptomatic individuals with stable plaques were included. All patients underwent 3.0T high-resolution MRI of the carotid artery (CA) for measuring the expansive remodeling (ER) ratio and assessing plaque stability. The ER ratio was calculated by dividing the maximum distance between the lumen and the outer border of the plaque in the internal CA by the lumen diameter within 1 centimeter of the plaque at the distal ipsilateral internal CA. ER ratios were compared between the symptomatic and asymptomatic groups. The 41 symptomatic patients were further divided into 4 groups according to stenosis rate (CA stenosis <50%, 50%–74%, 75–89%, and > 90%), and the correlation between the ER ratio and the rate of stenosis was evaluated.

Results: There was a significant difference in ER ratio between the symptomatic and asymptomatic groups (p<0.001). When symptomatic patients were divided into 4 subgroups based on degree of stenosis, ER ratios among groups showed statistically significant differences (p=0.014).

Conclusion: There were significant associations of the ER ratio with ischemic symptoms. Furthermore, the ER ratio in symptomatic patients continued to increase with stenosis severity. These findings suggested that the ER ratio might be a practical marker of plaque vulnerability in the CA and further prospective studies for asymptomatic patients are warranted.

Keywords: carotid stenosis; expansive remodeling; high-resolution MRI; vulnerable plaque; ischemic symptoms.

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Conflict of interest: There is no conflict of interest.
Funding: Grants from the Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (No.20152528); Shanghai Pujiang Program (16PJD036); Three-year plan program by Shanghai Shen Kang Hospital Development Center (16CR3043A); Shanghai Science and Technology Commission of Shanghai Municipality Program (14DZ1941206); the Cross Project of Medicine and Engineering from Shanghai Jiao Tong University (YG2015MS21) and Shanghai key discipline of medical imaging (No.2017ZZ02005).
Ethical approval: The study was approved by the ethical committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital
Informed consent: Informed consent was obtained from all individual participants included in the study

Journal of Interventional Medicine 2018;1(2): 82-85.

INTRODUCTION

Expansive remodeling (ER) is a common concept for coronary arteries, constituting a compensatory mechanism that reduces arterial stenosis caused by plaques (1). A considerable number of studies assessing the coronary artery indicated that positive remodeling has a close association with unstable lesions, which potentially cause ischemic events. Expansive remodeling is highly associated with plaque instability and high risk of developing ischemic events (2-4). Thus, expansive remodeling of the arteries plays an important role in atherosclerosis.

Previous studies have assessed the structural remodeling of carotid arteries (CAs) (5-8). However, relatively few reports have evaluated the arterial remodeling of carotid arteries quantitatively and its associations with plaque stability and stenosis severity. Currently, the main treatments for preventing future ischemic events include carotid endarterectomy, carotid artery stenting, and medical treatment, and are decided upon primarily based on the severity of stenosis. The current study aimed to assess the associations of expansive remodeling of CAs with ischemic events and the severity of carotid stenosis. The findings provide a more accurate risk stratification of carotid plaques for cerebral apoplexy prevention, and high risk patients would benefit more from early intervention.

MATERIALS AND METHODS

Patients and ischemia symptoms

Between 2015 and 2016, 41 symptomatic patients with vulnerable plaques and 25 asymptomatic individuals with stable plaques were included in this cross sectional study. The patients were diagnosed at the Department of Interventional Radiology of Shanghai No.6 Hospital. Ischemia symptoms included transient ischemic attack (TIA), ischemic stroke, or amaurosis fugax of the ipsilateral CA in the last 6 months; the symptoms were recorded based on detailed medical records. All patients underwent high-resolution MRI of the carotid artery at 3Tesla to assess plaque stability. According to the modified AHA Classification, plaques with possible surface defect, lipid-rich necrotic core, hemorrhage, or thrombus were considered to be vulnerable. The severity of CA stenosis was determined according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. Before MRI, the necessity and contradictions were explained, and informed consent was provided. This study was approved by the hospital ethics committee. Patients with poor imaging quality or near occlusion were excluded.

MR imaging protocol

All patients underwent high-resolution MRI of the carotid artery on a 3.0T MRI instrument (Siemens, Germany) with a dedicated 8-channel surface coil. The scans were centered on the carotid bifurcation. The parameters for imaging sequences were: 1) TR=29 ms and TE=4.17 ms for 3d TOF-MR-angiography; 2) TR=800 ms and TE=13 ms for axial pre-and post-contrast, in fat and blood suppressed 2D-T1 turbo-spin-echo sequence; 3) TR=3500 ms and TE=76ms for 2D-T2 turbo-spin-echo sequence. The total scan time was about 30 to 35 minutes per patient. Post-contrast T1W imaging was performed about 5 minutes after intravenous injection of Gadolinium-DTPA-BMA (Gadobutrol, Bayer-Schering, Leverkusen, Germany).

Data Analysis

Patient characteristics are shown as number (%) of cases and mean±standard deviation (SD). The Wilcoxon's signed-rank test and Welch's t-test were used to analyze differences between groups or within a given group. Data analysis was performed with SPSS for Windows, Version 19.0 (IBM, Chicago/IL, USA). Differences were considered statistically significant at $P<0.05$.

Measurement of expansive remodeling ratio (ERR)

The ER ratio was calculated by dividing the maximum distance between the lumen and the outer border of the plaque in the internal carotid artery (ICA) by the lumen diameter within 1 centimeter of the plaque at the distal ipsilateral ICA measured by 3d TOF imaging (Fig.1).

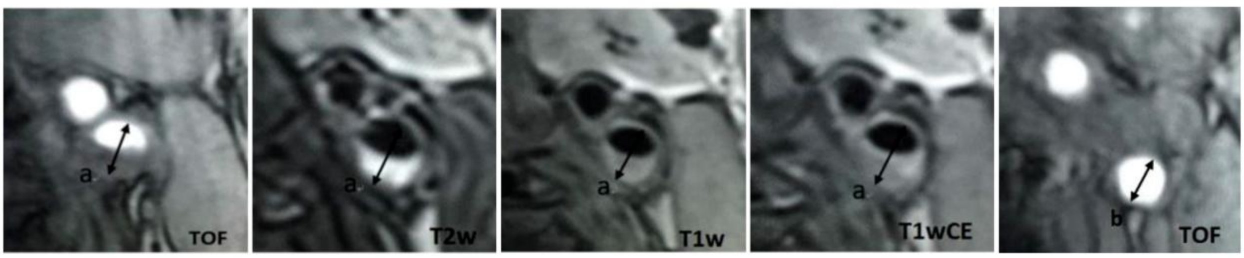

Figure 1. Measurement of the ERR by high-resolution MRI of the carotid artery at 3Tesla. ERR = maximum distance between the lumen and the outer border of the plaque in the ICA (a) divided by the lumen diameter within 1 centimeter of the plaque at the distal ipsilateral ICA measured on 3d TOF image (b) .

RESULTS

Table 1 compares possible influencing factors of ischemic events between the two groups. The results showed that none of them had a significant difference between symptomatic and asymptomatic patients, except for the rate of stenosis. Indeed, the two groups differed markedly in the percentage of stenosis (p=0.009). The mean stenosis rate was much higher in symptomatic patients than in asymptomatic individuals (65.6±19.9% vs.51.8±19.9%).

Table 1 Patient characteristics.

Characteristic	Symptomatic group	Asymptomatic group	P value
Number of patients	41	25	
Mean age ±SD	13 (31.7%)	5 (20.0%)	0.145
Females	9 (36%)	5 (20%)	0.397
Mean % stenosis ±SD	65.6±19.9	51.8±19.9	0.009 *
Hypertension	28 (68.3%)	14 (56.0%)	0.232
Hyperlipidemia	17 (41.5%)	9 (36.0%)	0.796
Diabetes	18 (43.9%)	9 (36.0%)	0.610
Smoking history	18 (43.9%)	9 (36.0%)	0.610

*Statistically significant difference between the 2 groups (p<0.05)

As shown in Fig 2, the ER ratio in symptomatic patients with vulnerable plaques was significantly different from that of asymptomatic patients with stable plaques. Next, the 41 symptomatic patients with vulnerable plaques were divided into 4 subgroups based on the percentage of luminal stenosis (CA stenosis <50%, 50%–74%, 75–89%, and >90%), and mean ER ratios were 1.393± 0.099 for CA stenosis <50% (n=8), 1.482±0.142 for the 50%–74% group (n=11), 1.501±0.161 for the 75%–89% group (n=12), and 1.630±0.166 for CA stenosis >90% (n=10). These findings suggested that ER ratios were significantly different among the 4 groups (p=0.014), as shown in Fig 3. Indeed, the ER ratio increased with the percentage of luminal stenosis.

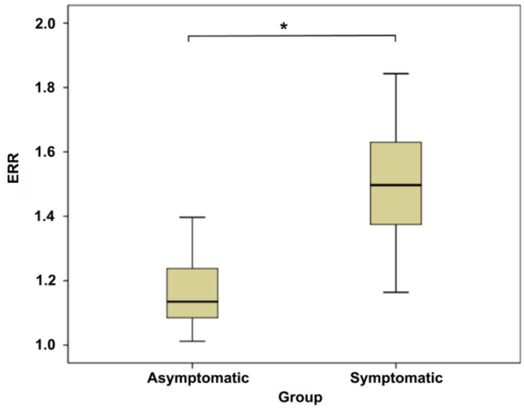

Figure 2. ER ratios of symptomatic (n=41) and asymptomatic (n=25) patients. The ER ratio of symptomatic patients (1.497±0.16) was significantly elevated compared with that of asymptomatic individuals (1.131±0.11) (*p<0.001).

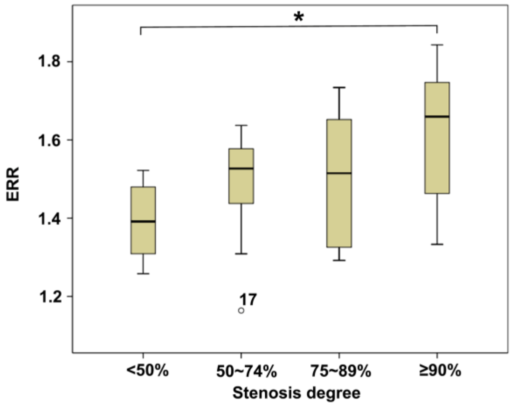

Figure 3. Subgroup analysis of ER ratios in symptomatic patients with vulnerable plaques divided into 4 groups based on percentage of luminal stenosis (CA stenosis <50%, 50%–74%, 75–89%, and >90%). ER ratios showed statistically significant differences among the 4 subgroups (*p=0.014).

DISCUSSION

Studies of coronary arteries have shown positive associations of expansive remodeling with unstable coronary events. Therefore, expansive remodeling is closely related to a higher risk of vulnerable plaques (9-12). According to previous studies, vulnerable plaques may contain a large necrotic lipid core with a thin or disrupted fibrous cap, potentially causing ischemic events; the fibrous cap is an important structure for plaque stability (13, 14). High-resolution MRI of the CA can detect the fibrous cap status and provide more precise information about the plaque component (15-17). A previous study reported that positive remodeling of plaques has tight associations with larger lipid cores and higher macrophage amounts compared with negatively or less positively remodeled plaques, suggesting that more extensively remodeled plaques tend to result in higher risk of vulnerability (18).

The ER ratio for coronary arteries is quantitatively measured mainly by intravascular ultrasonography (19). However, there are few studies of ER for carotid arteries utilizing high-resolution MRI. In this study, we aimed to assess the associations of expansive remodeling of carotid arteries with ischemic events (20). The NASCET criteria was used for stenosis assessment, with 3.0T high-resolution MRI of the CA utilized to detect plaques, as a simple and minimally invasive imaging method (21). In addition, it accurately detects plaque components and stability. According to the modified AHA classification, plaques with possible surface defect, hemorrhage, or thrombus are considered to be vulnerable.

In this study, possible influencing factors of vulnerable plaques were assessed, including hypertension, diabetes, and smoking history. The results showed that none of them was significantly different between symptomatic and asymptomatic patients, except for the degree of stenosis. The ER ratio in symptomatic patients with vulnerable plaques showed a statistically significant difference compared with that of asymptomatic patients with stable plaques. These findings suggest that the mechanisms of formation probably differ between vulnerable and stable plaques. When symptomatic patients with vulnerable plaques were classified into 4 groups based on the percentage of luminal stenosis, the ER ratio increased with the percentage of luminal stenosis. Moreover, ER ratios showed statistically significant differences among the 4 groups. Therefore, a high level of expansive remodeling of CAs and severe luminal stenosis might contribute to plaque instability, leading to ischemic events.

Besides MRI, other imaging methods can be used to assess the ER of the carotid artery as well, e.g. CA ultrasonography. Ultrasonography is non-invasive and convenient for repeated measurements, but hardly detects plaques at a high position. Our findings suggest that MRI plays an indispensable role in assessing vulnerable plaques as the only imaging technique for CA plaques detecting hemorrhage, lipid and necrotic core, and the status of the fibrous cap. Thus, evaluating the ER of carotid arteries combined with MRI for plaque features could reliably identify vulnerable plaques, which suggest possible future ischemic events.

However, MRI still has limitations. It is susceptible to movement artifacts, takes longer time for imaging, and has many contraindications. Patients with metal objects, such as pacemakers and artificial limbs or joints, are not eligible for magnetic resonance imaging.

The current study had limitations related to its cross sectional design, which is not a prospective analysis. To demonstrate the predictive value of the ER ratio for ischemic events, it is essential to carry out long-term prospective studies in asymptomatic patients with mild stenosis. Furthermore, the number of patients in the present study was relatively small, and further studies with more patients are required to validate our preliminary conclusion.

The ER ratio is significantly associated with ischemic symptoms. In addition, the ER ratio in symptomatic patients increases with the severity of stenosis. The present findings suggest that the ER ratio might be a practical marker of plaque vulnerability in the CA. To assess the predictive value of the ER ratio for future stroke events, it is essential to perform further prospective studies.

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