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Assessment of Mechanical Properties of Common Carotid Artery in Takayasu's Arteritis Using Velocity Vector Imaging

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Background: Alteration of arterial elastic properties is known to occur in patients with arteritis. Velocity vector imaging (VVI) is a new technology to assess multi-dimensional regional mechanics in terms of velocity, strain, strain rate and displacement. The aim of the present study was to investigate the mechanical properties of the common carotid artery using VVI in patients with Takayasu's arteritis (TA).

Methods and Results: Vascular properties of the carotid artery were assessed in 12 patients with TA (11 female, age 38±10 years) and 12 healthy age- and sex-matched controls. Velocity, strain, strain rate and displacement were decreased significantly in TA compared with controls. Standard deviations, however, of time to peak velocity (Tv), strain (Ts), strain rate (Tsr), and displacement (Td) of multiple arterial wall segments were significantly higher in TA (P<0.0001), suggesting disturbance of symmetric arterial expansion during systole. The severity of carotid stenosis was also positively correlated with standard deviations of Tv, Ts, Tsr and Td.

Conclusions: Arterial assessment using VVI may represent a new noninvasive method for quantifying vascular alteration associated with arteritis. (*Circ J* 2010; **74:** 1465–1470)

Key Words: Carotid arteries; Takayasu's arteritis; Ultrasonography

Takayasu's arteritis (TA) is a chronic inflammatory disease affecting the large elastic arteries occurring in the young. It results in occlusive or ectatic changes mainly in the aorta and its immediate branches as well as the pulmonary artery and its branches.[1,2] The disease is heterogenous in presentation and progression, and its course may be biphasic, with an early systemic phase characterized by nonspecific inflammatory features and a later stage reflecting occlusive lesions of the affected vessels.[1] It has been reported that widespread thickening of the walls of elastic arteries is one of the characteristics of TA.[3] Mechanical properties of the involved arteries, however, are not well known. Recently, velocity vector imaging (VVI), a novel method based on speckle tracking, has been suggested to be useful to assess multi-dimensional regional mechanics such as velocity, strain, strain rate and displacement,[4–7] thereby enabling rapid and accurate quantitative measurement of myocardial velocities, strain, and strain rate. In the present study we tested the application of this new method to evaluate regional vascular properties of carotid arteries, and hypothesized that systolic arterial expansion would be disturbed in patients with TA.

Methods

Study Subjects

The present study included 12 patients (11 female, age 20–54 years) with TA fulfilling the American College of Rheumatology criteria.[8] Patients with valvular heart disease and arrhythmia were excluded from the study. Two subjects were in an active stage of the disease, and the remaining 10 were in a quiescent stage. The control group, matched for gender and age, consisted of 12 individuals 21–50 years of age. Participants in the control group were individuals with no evidence of diabetes mellitus and no history of cardiovascular disease or hypertension, with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg, and the absence of carotid plaque on carotid ultrasonography. The present study was approved by the Institutional Review Board of Severance Hospital, Yonsei University College of Medicine, and informed consent was obtained from all study subjects.

Ultrasound

High-resolution B-mode carotid ultrasonography was per-

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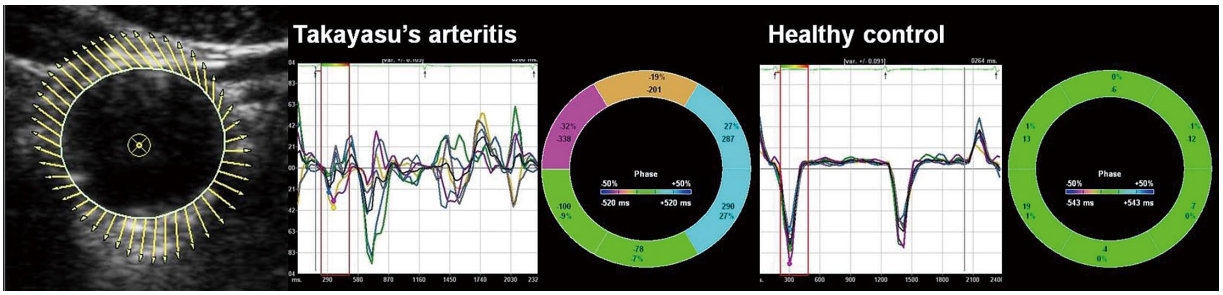

Figure 1. (**Left**) Velocity vector imaging (VVI) of carotid arterial wall and VVI maps displaying velocities throughout the cardiac cycle from 6 segments with segmental time to peak velocity in (**Middle**) a patient with Takayasu's arteritis and (**Right**) a healthy control.

Table 1. Subject Characteristics

	Takayasu's arteritis (n=12)	Controls (n=12)	P value
Age (years)	38±10	38±10	0.977
Female (%)	11(91.7)	11(91.7)	1.000
SBP (mmHg)	120±17	118±11	0.315
DBP (mmHg)	73±9	74±8	0.606
HR (/min)	73±8	71±9	0.898
BMI (kg/m^2)	22.0±2.7	20.7±1.7	0.590

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; BMI, body mass index.

formed using a linear array 8-MHz transducer. The right and left common carotid arteries were examined with the head tilted slightly upward in the midline position. The scan was performed in both transverse and longitudinal planes. Intima–media thickness (IMT), external diameter and internal diameter of both common carotid arteries were measured in the longitudinal plane at both peak systole and diastole using B-mode echocardiography. The carotid IMT was semi-automatically measured with the Syngo Arterial Health Package (Siemens Medical Solutions USA, Mountain View, CA, USA). Mean carotid IMT was calculated automatically on all the frames within a single region of interest (1-cm length) selected by the user 1 cm distal to the bulbs. Luminal stenosis was calculated as the percent ratio of internal diameter to external diameter at peak diastole. Carotid luminal strain, the percent systolic expansion of the arterial lumen, was calculated as luminal strain=([internal diameter at peak systole−internal diameter at peak diastole]/internal diameter at peak diastole)×100.[9]

The VVI was performed on digitally acquired images on Sequoia ultrasound systems (Siemens Medical Solutions USA Inc, Mountain View, CA, USA). Syngo Velocity Vector Imaging technology (Siemens Medical Solution USA Inc) was used to display and measure global and regional mechanics of the common carotid arterial walls. All measurements were performed in a stepwise manner as follows. First, high-quality images from the transverse plane of a common carotid artery approximately 1.5 cm from the bifurcation to the aortic arch, and a single beat acoustic capture were done. Second, the media–adventitia interface of the carotid arterial wall was manually traced from a still frame image and automatically tracked by the software. The intima-media complex was visually distinguished from high-echogenic adventitia and other surrounding tissues. Repeated tracing was sometimes performed to optimize accurate border tracking of the intima–media complex, and tracing was accepted only when the VVI visual display mode accurately identified borders throughout the cardiac cycle. Third, display of the direction and magnitude of tissue velocities throughout the cardiac cycle was obtained with the frame of reference at the center of the artery. The software divides arterial wall into 6 segments for analysis. Fourth, measurement of peak radial velocity, circumferential strain, circumferential strain rate, radial displacement, time to peak systolic velocity (Tv), time to peak strain (Ts), time to peak strain rate (Tsr) and time to maximal displacement (Td) was performed in each segment. The average values of all segments were used to represent peak radial velocity (Pv), circumferential strain (Ps), circumferential strain rate (Psr) and radial displacement (Pd) of the arteries. The standard deviations of Tv, Ts, Tsr and Td (Tv-SD, Ts-SD, Tsr-SD and Td-SD) of 6 segments were used as indicators of dyssynchronous arterial expansion during systole (**Figure 1**). Intra- and interobserver variability for measurement of VVI imaging were determined by analysis of 10 random images by one observer (blinded to the first analysis with 1-month interval) and additional image analysis of a second observer (blinded to the results from the first observer).

Statistical Analysis

Means and standard deviations were calculated for continuous variables. To determine whether the severity of carotid luminal narrowing correlated with parameters of dyssynchronous arterial expansion, the Pearson correlation coefficient was calculated. An unpaired t-test was performed to compare the study population with the control group and to examine differences in parameters assessed on VVI. Intra- and interobserver variability for parameters obtained on VVI was studied by calculating the coefficient of variation (defined as the standard deviation of the differences between the two series of measurements divided by the mean of both measurements). $P<0.05$ was considered statistically significant.

Results

The baseline characteristics were largely comparable between the groups (**Table 1**). In 1 patient with TA, the left common carotid artery could not be visualized because it was completely occluded. Therefore, a total of 23 arteries

Table 2. VVI: Arterial Wall Thickness and Arterial Wall Motion of Common Carotid Arteries

	Takayasu's arteritis	Controls	P value
No. examined carotid arteries	23	24	
Intima-media thickness (mm)	1.16±0.48	0.46±0.07	<0.0001
Internal diameter (mm)	4.24±2.07	5.93±0.64	0.001
External diameter (mm)	6.41±1.55	6.70±0.72	0.415
Luminal stenosis (%)	37±22	12±2	<0.0001
Luminal strain (%)	4.16±4.15	8.66±3.34	<0.0001
Pv (mm/s)	1.17±1.36	1.42±0.59	0.032
Ps (%)	3.58±2.99	4.99±2.05	0.015
Psr (/s)	0.23±0.18	0.39±0.18	0.004
Pd (mm)	0.15±0.06	0.31±0.20	0.007
Tv-SD (ms)	38.2±26.4	13.3±10.0	<0.0001
Ts-SD (ms)	199.3±93.7	87.1±58.4	<0.0001
Tsr-SD (ms)	74.9±34.8	28.7±19.4	<0.0001
Td-SD (ms)	125.4±93.1	41.9±36.4	<0.0001

VVI, velocity vector imaging; Pv, peak radial velocity; Ps, peak circumferential strain; Psr, peak circumferential strain rate; Pd, peak radial displacement; Tv-SD, standard deviation of time to peak radial velocity; Ts-SD, standard deviation of time to peak circumferential strain; Tsr-SD, standard deviation of time to peak circumferential strain rate; Td-SD, standard deviation of time to peak radial displacement.

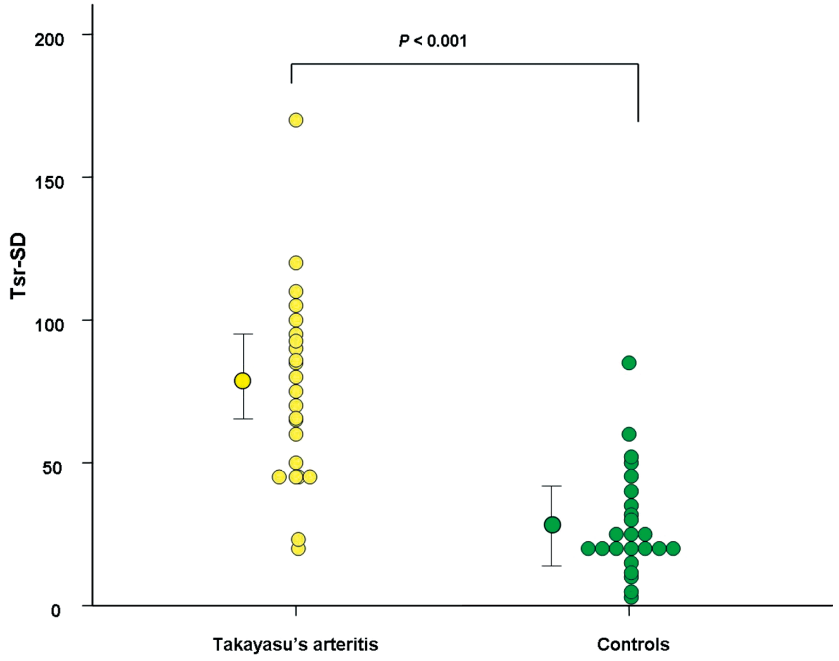

Figure 2. Standard deviation of Tsr in patients with Takayasu's arteritis and healthy controls. No significant overlap between Takayasu's arteritis and control. Tsr-SD, standard deviation of time to peak circumferential strain rate.

from TA subjects and 24 arteries from healthy control were studied.

The mean IMT of carotid arteries in patients with TA was significantly higher than that of the controls (1.16±0.48 mm vs 0.46±0.07 mm, P<0.0001). Internal diameter of the carotid arteries was decreased (4.24±2.07 mm vs 5.93±0.64 mm, P=0.001), and the luminal stenosis was more severe in TA compared with controls (37±22% vs 12±2%, P<0.0001). None of the subjects in the control group had luminal narrowing of carotid arteries >50%, whereas 4 common carotid arteries (17.4%) had luminal narrowing >50% in patients with TA. Luminal strain was also decreased in TA (4.16±4.15 vs 8.66±3.34%, P<0.0001).

Pv (1.17±1.36 mm/s vs 1.42±0.59 mm/s, P=0.032), Ps (3.58±2.99% vs 4.99±2.05%, P=0.015), Psr (0.23±0.18/s vs 0.39±0.18/s, P=0.004) and Pd (0.15±0.06 mm vs 0.31±0.20 mm, P=0.007) decreased significantly in patients with TA when compared with controls, suggesting reduction in outward expansion. But Tv-SD (38.2±26.4 ms vs 13.3±10.0 ms), Ts-SD (199.3±93.7 ms vs 87.1±58.4 ms), Tsr-SD (74.9±34.8 ms vs 28.7±19.4 ms) and Td-SD (125.4±93.1 ms vs 41.9±36.4 ms) were significantly higher in patients with TA when compared with controls (P<0.0001), suggesting disturbance of symmetric arterial expansion during systole (Table 2). Among the variables, Tsr-SD was the most useful parameter in discriminating patients with TA from healthy controls and there was no significant overlap between the groups (Figure 2). The severity of carotid luminal stenosis was positively correlated

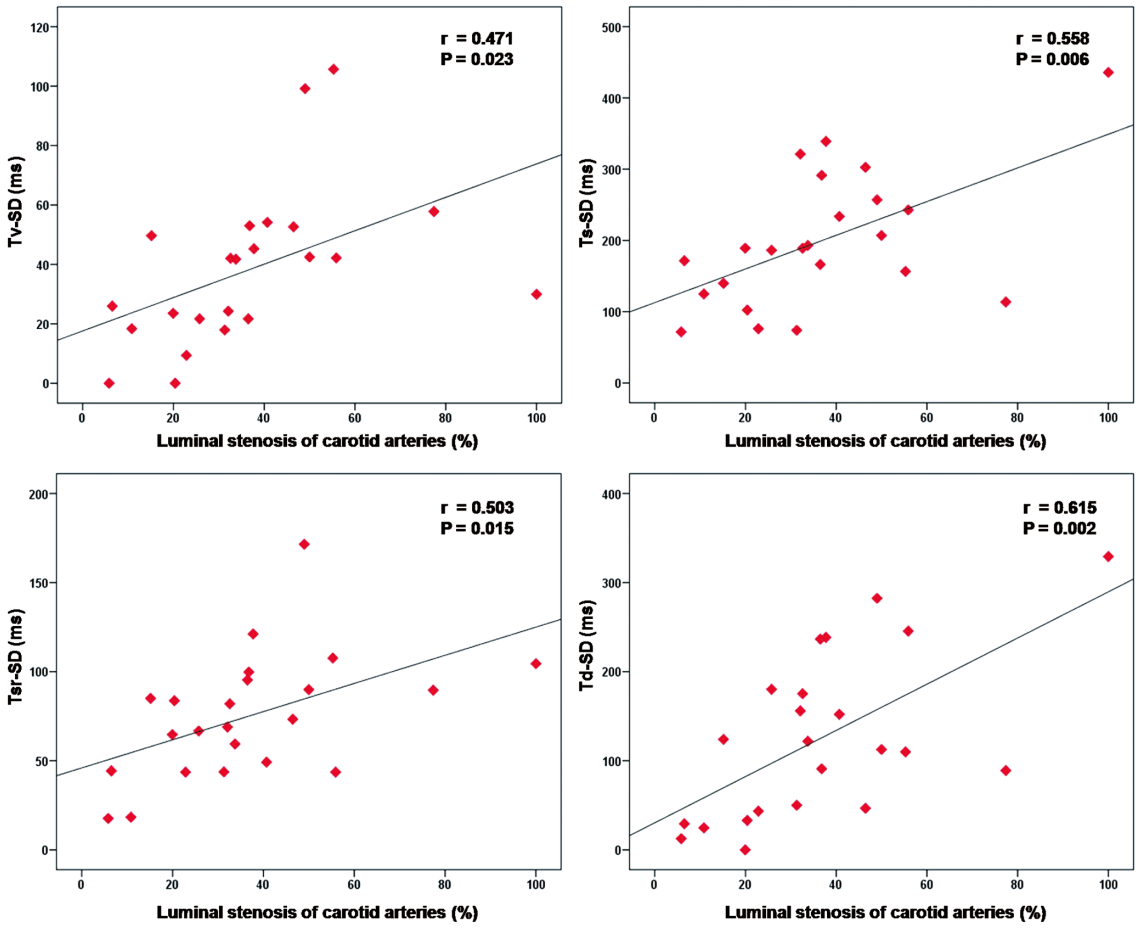

Figure 3. Correlation between the severity of luminal stenosis in carotid arteries and the parameters reflecting dyssynchronous expansion in Takayasu's arteritis. Correlation coefficient (r) and probability of any significant correlation using 95% confidence (P) are indicated in each diagram. Td-SD, standard deviation of time to peak radial displacement; Ts-SD, standard deviation of time to peak circumferential strain; Tsr-SD, standard deviation of time to peak circumferential strain rate; Tv-SD, standard deviation of time to peak radial velocity.

with Tv-SD, Ts-SD, Tsr-SD and Td-SD in patients with TA (Figure 3). Furthermore, Pv, Ps, Psr and Pd were all positively correlated with carotid luminal strain (r=0.328, r=0.474, r=0.375 and r=0.533, respectively, P<0.05), which reflects arterial distensibility.

Intraobserver variability was 5.1±3.4% for Pv, 8.4±5.3% for Ps, 5.0±4.3% for Psr, 4.6±3.1% for Pd, 7.3±8.3% for Tv-SD, 6.0±2.8% for Ts-SD, 9.2±3.0% for Tsr-SD, and 9.3±5.5% for Td-SD. The corresponding values for interobserver variability were 7.1±4.5%, 8.7±5.1%, 6.0±4.0%, 5.2±5.2%, 8.8±7.0%, 9.1±6.0%, 10.3±3.6% and 9.7±6.2%, respectively. The intra- and interobserver variability was evaluated on Bland–Altman plot for Tsr-SD. The mean differences were –1.41 ms (95% confidence interval (CI): –5.44 to 2.61 ms) for the same observer, and 0.04 ms (95%CI: –4.66 to 4.73 ms) for different observer, respectively.

Discussion

The principal findings of the current study are (1) carotid arteries of patients with TA have abnormal mechanical properties characterized by reduced and dyssynchronous arterial expansion during systole; and (2) the degree of dyssynchronous expansion is positively correlated with the severity of carotid arterial luminal narrowing. These findings suggest that arterial assessment using VVI may represent a new method for non-invasively quantifying vascular alteration associated with arteritis.

The basic pathological process that results in TA is chronic inflammation of arterial walls, which causes structural changes. Macroscopically, the arterial wall is thickened secondary to fibrosis of all three vessel layers and the lumen is narrowed in a patchy distribution. Histologically, inflammation starts in the media and the adventitia, and reactive fibrocellular thickening of the intima occurs in response to the destruction of the media and adventitia.[10] In the later stage of the disease, there is a predominance of the fibrous component and gradual progression to scarring and shortening of affected vessels.[11,12]

Common carotid artery is frequently involved in TA and it has been observed in 60–70% of TA cases.[13] Ultrasonography is a non-invasive and effective method for evaluating carotid arteries.[14] It has been reported that B-mode ultrasonography was able to visualize the classical caliber abnor-

malities in TA and depicted vessel wall thickening.[11,12] Although morphological changes assessed on ultrasonography have been well characterized, functional evaluation of arterial wall is still challenging. Stiffness index of carotid artery has been reported to be significantly higher in TA than in normal subjects.[15] Similarly, elevated arterial stiffness in the central aorta has been demonstrated in patients with TA and it may persist even when the disease is quiescent.[16] Because arterial changes in arteritis are not uniform through the whole arterial circumference, methods to detect local vascular changes would be more helpful. Regional mechanics of the arterial wall during systole in patients with arteritis, however, is not well understood due to technical difficulties.

Recently it has been reported that the properties of the carotid artery wall could be directly characterized by using strain rate imaging, based on tissue Doppler imaging.[17] Doppler-derived techniques, however, are angle-dependent, and it is also difficult to evaluate regional mechanics of arterial wall with this technique. VVI is a novel method for detecting tissue pixels and tracking these acoustic markers from frame to frame. This method has an advantage of measuring velocity and deformation, not depending on the incident angle of the ultrasound beam.[4–7] VVI has been applied to evaluate left ventricular myocardial mechanical performance, but it can also be useful in assessing the multi-dimensional regional mechanics of large vessels in a transverse plane, using ultrasonography images. In the present study VVI was used to evaluate the motion of arterial wall affected by TA. We found that peak radial velocity, circumferential strain, circumferential strain rate, and radial displacement during systolic phase in TA were distinctly lower than in controls, suggesting impaired arterial expansion. These findings are consistent with previous studies showing impaired arterial elasticity in TA.[15,16] Impaired arterial properties in TA observed in the present study may be related to inflammatory changes in artery walls, which would have reduced the capacity for elastic recoil and hence would permit gradual plastic deformation and outward expansion of the artery.

A more important finding from the present study is that arterial expansion is not only reduced but also does not uniformly take place in patients with TA, although the arterial lumen is shown to be uniformly thickened by B-mode echocardiography. Dyssynchronous arterial wall expansion during systole will produce disturbed local blood flow. This turbulent flow will increase areas of arterial wall exposed to oscillatory shear stress. These areas are the most prone to development of intimal thickening and atherosclerosis. In combination with endothelial dysfunction, these abnormalities are likely to be important in the accelerated atherosclerosis in TA.[18,19]

In the present study the severity of luminal narrowing in carotid arteries was positively correlated with degree of dyssynchronous expansion. These findings could support the relationship between abnormal arterial mechanical property and luminal narrowing in patients with TA. TA produces thickening and altered echogenity of the media, adventitia and peri-arterial tissues even in some portions of the aorta, which looked normal on angiography.[20] The mural thickness of carotid arteries affected by TA closely correlates with severity of luminal stenosis. Thus, the degree of dyssynchronous expansion during systole may be considered as a marker of vascular alteration in TA, and allow early detection of altered arterial performance in arteries affected by inflammatory diseases.

The main limitation of the present study was the small number of patients, reflecting the rarity of TA. It is also unknown whether parameters of VVI can distinguish between active and inactive forms of the disease. 2-D speckle tracking algorithms used in VVI are dependent on image quality and intima–media complex border definition. Therefore, good image quality was required for analysis, although no data were excluded in the present study due to suboptimal tracking by VVI. To our knowledge the present study is the first to use VVI for arterial wall evaluation. According to the present results, the variability of the parameters obtained by VVI is reasonable, and VVI can be used for the assessment of arterial characteristics.

Conclusion

VVI can be applied to evaluate vascular alteration associated with arteritis in humans. This diagnostic method is inexpensive, non-invasive, and performed quickly and easily. In patients with TA, the carotid artery had dyssynchronous arterial expansion during systole when compared with healthy controls. In addition, the degree of dyssynchronous expansion was positively correlated with the severity of carotid luminal stenosis. Therefore, arterial assessment using VVI may represent a new non-invasive method for quantifying vascular alteration associated with arteritis.

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