Arterial wall thickness measurements by B mode ultrasonography in patients with Takayasu's arteritis

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Abstract

***Objective*—To assess the feasibility and potential diagnostic usefulness of arterial ultrasonography in Takayasu's arteritis.**

***Methods*—The total wall, intimal + medial, and adventitial thickness of the common carotid, subclavian and common femoral arteries, and of the abdominal aorta, were examined by B mode ultrasonography in 16 patients with Takayasu's arteritis and 16 healthy control subjects.**

***Results*—The mean total wall and intimal + medial thickness of all arteries other than the common femoral were significantly increased in Takayasu's arteritis. Long segments of homogeneous circumferential wall thickening in multiple vessels were characteristic.**

When the common carotid and subclavian arteries and the abdominal aorta were examined, each individual with Takayasu's arteritis had at least one artery with total wall thickness exceeding the reference range in controls.

***Conclusions*—B mode ultrasonography is able to expose the widespread arterial wall thickening characteristic of Takayasu's arteritis and may provide a useful tool for the detection and follow up of this disease.**

(*Ann Rheum Dis* 1996; 55: 461–465)

Takayasu's arteritis is a chronic inflammatory arteriopathy of unknown aetiology that preferentially affects the major elastic arteries such as the aorta, its main branches, and the pulmonary arteries.[1 2] It often afflicts women during their reproductive years. The disease is heterogeneous in presentation and progression, and its course may be biphasic, with an early systemic phase characterised by non-specific inflammatory features and a later stage reflecting occlusive lesions of the affected vessels.[2] Diagnosis of Takayasu's arteritis is frequently difficult and the time from onset of symptoms to diagnosis is usually long.[3 4] The media and adventitia of the arterial walls are involved predominantly, with intimal thickening and arterial occlusions occurring as important late phenomena.[5] During the early active stage of the disease, arterial biopsy shows granulomatous inflammation and patchy destruction of the medial musculoelastic lamellae.[6] The microscopic changes later become non-specific and consist of sclerosing arteritis, fibrous intimal hyperplasia, medial scarring, and adventitial fibrosis.[1 4] Many patients, however, continue to have active or low level disease over extended periods of time, and many of the lesions in these patients may in fact be a mixture of fibrosis, intimal proliferation, and intermittent chronic inflammatory changes.[3] Our ability to detect active disease is severely limited, as many patients who appear to be in an inactive phase of disease or in remission may in fact present inflammation of the vessel wall at bypass surgery.[3 7]

Takayasu's arteritis is usually diagnosed by means of contrast angiography.[8–10] This technique, however, does not reveal involvement of the arterial wall, but only visualises the resultant luminal narrowings and dilatations. Transcutaneous B mode ultrasound is capable of demonstrating the wall thickness and the three layer structural composition of the walls of large superficial arteries with high precision.[11–14] The diagnostic value of ultrasonography in Takayasu's arteritis is still poorly known, though several promising but small reports exist.[15–19] In the present study, we have evaluated the clinical usefulness of transcutaneous B mode ultrasound in Takayasu's arteritis, focusing on measurement of the thickness of the wall of the carotid, subclavian and femoral arteries, and of the abdominal aorta, in patients with established arteritis.

Patients and methods

PATIENTS AND CONTROLS

All patients and control subjects were Finnish. The study group consisted of 16 patients (14 women) 21–66 years of age (mean age 45·7 years). In each of them, the diagnosis of Takayasu's arteritis was based on a history and clinical findings suggestive of systemic disease, and on angiography; the time since diagnosis averaged 16·4 years (range 5–36 years). At the time of our study, four patients showed symptoms or signs of an active inflammatory process and were receiving corticosteroid treatment. The remaining 12 patients were considered to be in the late, non-active phase of the disease; five had previously received corticosteroids. At angiography, total occlusions or stenoses >50% of the luminal diameter were identified in the carotid arteries in seven patients, in the subclavian arteries in 13

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Accepted for publication 29 February 1996

patients, in the common femoral arteries in two patients, and in the abdominal aorta in four patients; seven patients had undergone vascular surgery for total occlusions. No patient had hypercholesterolaemia or diabetes, but seven individuals had hypertension and one was a smoker.

The control group, matched for gender and age, comprised 16 individuals (14 women) 25–64 years of age (mean age 46·4 years). All were asymptomatic and had neither history nor signs of atherosclerosis, hypertension, diabetes, or other systemic diseases; one was a smoker.

ULTRASOUND EXAMINATION

The left and right common carotid, subclavian, and common femoral arteries, in addition to the abdominal aorta, were examined with B mode ultrasonography, using an Acuson 128XP/10 scanner (Mountain View, CA, USA) with the subject in a supine position. The superficial arteries were examined using a 7 MHz linear array transducer, and the aorta with a 3·75 MHz sector transducer. The studies were recorded on videotape (Panasonic AG 7330 Super-VHS) and on radiographic film. Imaging of the common carotid arteries was performed in the antero-oblique, lateral, and postero-oblique projections, while the aorta and the common femoral and subclavian arteries were scanned in the anteroposterior and antero-oblique projections. Direction of the ultrasound beam was made as perpendicular to the arterial wall as possible, with the focus zone indicator in the middle of the arterial lumen, and compression of the vessel was avoided. Although our emphasis was on measuring arterial wall thickness, arterial stenoses and dilatations were also noted.

The ultrasound image of the arterial wall, but not that of the aortic wall, typically consisted of two echogenic lines with a hypoechogenic space between. The gain setting was adjusted so that the outer border of the outer echogenic line was as sharp as possible. The wall thickness measurements were made using a ruler with 0·13 mm increments and with a ×4 magnifying glass on the radiographic films, selecting the thickest site of the wall in a longitudinal view through the midline of the artery. The intimal + medial thickness was taken to be the combined width of the inner echogenic line and the hypoechogenic space, and the total wall thickness (intima + media + adventitia) was determined by including the outer echogenic line in the measurement. Both the intimal + medial width and total wall thickness could be determined in the common carotid, femoral, and subclavian arteries, while in the abdominal aorta only the total thickness was measurable. The near and far walls were analysed separately in each artery. No statistically significant differences occurred between the thickness measurements of the near and far walls in any artery, and these data were therefore averaged for each artery examined.

The repeatability of the measurements was assessed by twice measuring blindly the wall thickness of the common carotid and subclavian arteries in eight randomly selected individuals;[20] 32 arteries were analysed. The mean difference (SD) of the paired data was 0·04 (0·19) mm (95% confidence intervals (CI) −0·33 to +0·43 mm) for the thickness of the intima + media and 0·03 (0·23) mm (95% CI −0·42 to +0·48 mm) for the total wall thickness. The standard deviation of the difference calculated as a percentage of the average wall thickness was 9·6% for the intima + media and 9·2% for the total wall.

STATISTICS

Comparisons of the means of continuous variables between the Takayasu's arteritis and control groups and within each group were made with two sided Student's non-paired and paired t tests, respectively, and frequency data were analysed using Fisher's exact test; the data are given as mean (SD). The upper limits of normal arterial wall thicknesses were calculated as mean +2SD in the control group ($n = 16$). Values of $p < 0·05$ were considered statistically significant.

Results

The figure shows examples of arterial images in patients with Takayasu's arteritis and in the healthy controls. In both groups, the basic three layer ultrasound pattern of the arterial wall was well discernible in the carotid and femoral arteries, less distinct in the subclavian arteries, and could not be seen in the abdominal aorta. Visualisation of the proximal abdominal aorta was restricted by bowel gas in seven patients and five controls; in these subjects, the thickest visible arterial wall site was measured also. A long, continuous, circumferential and homogeneous thickening of the wall was a characteristic finding in Takayasu's arteritis and this was seen in all affected vessels.

The hypoechoic space of the wall, representing the media, was the most clearly thickened layer (figure) and was also slightly more echogenic in patients with Takayasu's arteritis than in the control subjects. Bright areas with shadows suggestive of arterial wall calcifications were seen more often in patients than in the control group (11 of 16 compared with three of 16; $p = 0·011$). The ultrasound findings in patients with symptoms and signs of the active disease did not differ from those in other patients.

Table 1 summarises the data and compares the Takayasu's arteritis and control groups. The mean total wall thicknesses of the carotid and subclavian arteries and of the abdominal aorta were significantly increased in subjects with Takayasu's arteritis. The group differences were most conspicuous in the left carotid and subclavian arteries. The differences in intimal + medial thickness were comparable to those in total wall width. Although similar trends were also observed in the femoral

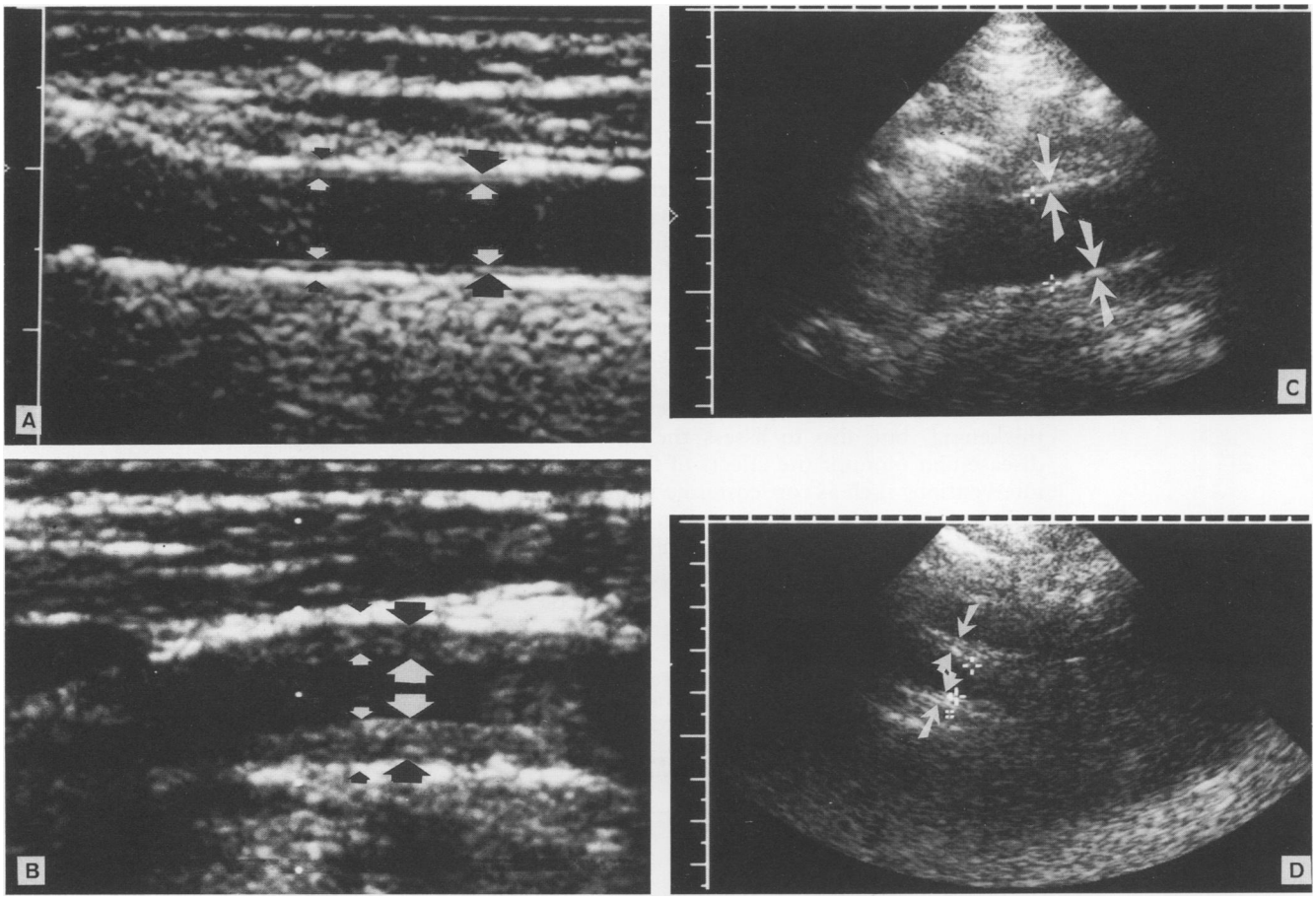
arteries, these did not attain statistical significance. The differences in the adventitial thickness were clearly less conspicuous and were statistically significant only in the left common carotid and left subclavian arteries.

In addition to comparing the group mean wall thicknesses, we determined the frequency and localisation of abnormally thickened arteries in the Takayasu's arteritis group. The upper 95% confidence limits of total wall thicknesses in the control group were 1·59, 1·67, 1·67, and 2·80 mm for the carotid, subclavian and femoral arteries, and abdominal aorta, respectively. Table 2 shows the distribution of wall thickening in the arteries examined in patients with Takayasu's arteritis. The data indicate that 94% of patients had either carotid or subclavian arteries with wall thickness exceeding the normal upper limit, and that the abnormality rate increased to 100% if the abdominal aortic data were also considered. Two fusiform dilatations occurred in the carotid arteries (6%), four aneurysms in the subclavian arteries (13%), and two aneurysms in the abdominal aorta (13%).

Discussion

Our data show that B mode ultrasonography is capable of exposing the widespread thickening of the walls of elastic arteries that is characteristic of Takayasu's arteritis. No statistically significant difference occurred among the groups in the femoral arteries, which are rarely affected in Takayasu's arteritis.[1] The increased thickness of the arterial wall in patients with Takayasu's arteritis resulted mainly from intimal + medial thickening, while the adventitial changes were less clearly consistent. In the abdominal aorta, only total wall thickening was recorded; the three layer wall structure could not be identified because of the limited resolution of the 3·75 MHz transducer. Although B mode ultrasound has been used increasingly in studies of carotid atherosclerosis in man,[21–23] its reported applications in Takayasu's arteritis hitherto are limited to a few case histories[15–18] and a study of carotid arteries in 23 patients.[19] In common with our present observations, a long, diffuse, and circumferential wall thickening of the large arteries in the upper body was the primary finding in all reports.

The suspicion of Takayasu's arteritis usually arises from clinical and laboratory findings of a systemic disease, but the diagnosis is often difficult. The presence of Takayasu's arteritis cannot be confirmed without imaging the arteries, usually by contrast angiography.[24 25] Delay in diagnosis in children was long in a study reported by Kerr *et al*, and may have been caused by a hesitancy on the part of



Comparison of artery walls by B mode ultrasonography in healthy controls and in patients with Takayasu's arteritis (TA), showing typical diffuse, circumferential arterial wall thickening in TA. Wall thickness was measured in the near and far walls except for the aorta, in which only total wall thickness was measured. ***A:*** *Common carotid artery in a healthy control.* ***B:*** *Common carotid artery in a patient with TA.* ***C:*** *Abdominal aorta in a healthy control.* ***D:*** *Abdominal aorta in a patient with TA.* ***A, B:*** *Distance between thick arrows = intimal + medial thickness; distance between thinner arrows = total wall thickness.*

Table 1 Arterial wall thickness at different sites of the body in patients with Takayasu's arteritis (TA) and in healthy controls

Artery	Layer of the artery	Wall thickness (mm)		
		Patients with TA	Controls	P
Right common carotid artery	Intima + media	1·23 (0·52)	0·74 (0·14)	0·001
	Adventitia	0·68 (0·21)	0·60 (0·10)	0·113
	Total	1·91 (0·61)	1·35 (0·13)	0·001
Left common carotid artery	Intima + media	1·75 (0·86)	0·74 (0·11)	0·0001
	Adventitia	0·69 (0·18)	0·58 (0·14)	0·029
	Total	2·44 (0·99)	1·32 (0·13)	<0·001
Right subclavian artery	Intima + media	2·08 (1·26)	0·87 (0·14)	<0·001
	Adventitia	0·49 (0·16)	0·51 (0·17)	0·395
	Total	2·57 (1·31)	1·38 (0·16)	0·001
Left subclavian artery	Intima + media	2·43 (1·06)	0·85 (0·17)	<0·0001
	Adventitia	0·57 (0·17)	0·50 (0·16)	0·114
	Total	2·99 (1·06)	1·35 (0·16)	<0·0001
Right common femoral artery	Intima + media	1·16 (0·60)	0·90 (0·18)	0·057
	Adventitia	0·51 (0·09)	0·52 (0·10)	0·375
	Total	1·66 (0·63)	1·42 (0·12)	0·066
Left common femoral artery	Intima + media	1·04 (0·39)	0·85 (0·18)	0·045
	Adventitia	0·53 (0·15)	0·52 (0·09)	0·332
	Total	1·57 (0·48)	1·37 (0·17)	0·065
Abdominal aorta†	Total	3·92 (1·88)	2·20 (0·31)	0·001

Values are mean (SD) arterial wall thickness, determined as the mean of the near and far walls except for †abdominal aorta—only the total thickness determined.

paediatricians to request diagnostic angiographic studies.[3] Intravenous digital subtraction angiography is less invasive than direct arteriography, but does not guarantee high quality visualisation of the vessel lumen and wall thickness.[4] Magnetic resonance imaging and computed tomography have also been introduced as diagnostic techniques in Takayasu's arteritis.[26–29] These methods are accurate in aortic studies, but less so in more distal arteries. Case reports exist that describe a decrease in aortic wall thickening detected after steroid treatment.[30 31]

In addition to earlier ultrasound reports,[15 19] our findings of arterial wall thickness suggest that B mode ultrasonography can provide useful diagnostic information in Takayasu's arteritis. Merely by studying the carotid arteries, we were able to identify 75% of our patients as having abnormal arterial wall thickening, while additional examination of the subclavian arteries and the abdominal aorta increased the revealed abnormality rate to 100%. It is noteworthy that the upper limits of normal arterial wall thickness in our present study were in close agreement with the data of other investigators.[19 32] B mode ultrasound could be used not only to detect the wall thickening, but also to assess the extent of disease and monitor the effects of therapeutic interventions such as corticosteroid treatment.

Although our data are promising, the design and size of the study did not allow a full evaluation of the diagnostic usefulness, including sensitivity and specificity, of B mode ultrasound in Takayasu's arteritis. The adventitial layer did not differ between patients and controls, and it remains unknown whether this method can distinguish arterial wall abnormalities attributable to Takayasu's arteritis from those reflecting simple atherosclerotic involvement. It is likewise unknown whether ultrasound can distinguish between the active and inactive forms of the disease. For these purposes, considerably larger studies are needed, focusing on patients with clinical suspicion of arteritis.

Table 2 Frequency of abnormally thickened arterial walls in 16 patients with established Takayasu's arteritis

Artery	Patients with increased wall thickness*	
	No	%
Left or right carotid artery	12	75
Left or right subclavian artery	14	88
Abdominal aorta	10	63
Left or right femoral artery	4	25
Carotid or subclavian artery	15	94
Carotid or subclavian artery or abdominal aorta	16	100

*The upper limit of normal wall thickness of each artery was the mean + 2 SD of the control group.

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