American Journal of Pathology, Vol. 139, No. 5, November 1991

Effect of Aging on Aortic Morphology in Populations with High and Low Prevalence of Hypertension and Atherosclerosis

Comparison Between Occidental and Chinese Communities

Renu Virmani,* Albert P. Avolio,† Wolfgang J. Mergner,* Max Robinowitz,* Edward E. Herderick,‡ J. Fredrick Cornhill,‡ Shou-Yen Guo,‖ Tong-hua Liu,¶ De-Yao Ou,# and Michael O'Rourke†

From the Department of Cardiovascular Pathology, Armed Forces Institute of Pathology, Washington, DC; The Department of Medicine,† University of New South Wales, St. Vincents Hospital, Darlinghurst, New South Wales, Australia; The Biomedical Engineering Center and Department of Surgery,‡ The Ohio State University, Columbus, Ohio; Department of Pathology,‖ Shanghai Second Medical College, Shanghai, China; Department of Pathology,¶ Peking Union Medical College Hospital, Beijing, China; and Department of Pathology,# Guangzhou Provincial People's Hospital, Guangzhou, China*

A comparative morphologic study of aortic changes with aging was conducted in different populations in an attempt to separate the effects of hypertension and atherosclerosis. Chinese and the occidental populations were chosen, as they are known to have a high prevalence of hypertension and atherosclerosis, respectively. Aortic tissue was collected from occidental (American and Australian) and Chinese populations from three geographic locations. Postmortem specimens were obtained from four fixed locations: ascending aorta (A), descending thoracic aorta (B), and abdominal aorta (suprarenal [C] and above the aortic bifurcation [D]). Histologic sections were used to measure aortic circumference, medial thickness, intimal thickness, and grade of atherosclerosis. Kidney sections were used to confirm the presence or absence of hypertension. A total of 302 cases (age range, 19 to 104 years; Male-to-female ration, 2:1) were studied: 112 Americans, 80 Australians, and 110 Chinese. Cases were divided into three age groups: 19 to 44; 45 to 64; and 65 years and older. The aortic circumference progressively decreased from sites A to D in all populations and age groups. The aortic circumference increased with age, and the increase was independent of the aortic location. When the populations were separated, however, the greater increase was at location A in the Chinese (P = .008) and locations D in the occidental (P = .13), a population contrast that was significant only in location A. Intimal thickness increased with advancing age and was maximal in the abdominal aorta. The population differences also were significant for intimal thickness and were significantly greater in the occidental population in B, C, and D locations, whereas for atherosclerosis significance was only seen in location D. Hypertension (as defined by the morphologic changes in the kidney) after adjusting for age, height, and weight resulted in no statistical significant effect on aortic circumference or on intimal thickness, but did show a significant increase in atherosclerosis score at locations B, C, and D. Also after adjusting for age, height, and weight, the Chinese had a significantly larger aortic circumference in location A compared with the occidental population, whereas in location D the occidentals with hypertension had a significantly larger circumference

Supported in part by Grant RO1 AG06942 from the National Institute on Aging, NIH, Bethesda, Maryland.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Army, Navy, or Department of Defense.

Accepted for publication June 28, 1991.

Address reprint requests to Renu Virmani, MD, Department of Cardiovascular Pathology, Armed Forces Institute of Pathology, Washington, DC 20306.

compared with Chinese, probably due to an interaction of atherosclerosis and hypertension. After similar adjustments, the medial thickness in locations A and C, the intimal thickness in B, C, and D, and atherosclerosis score in D were significantly greater in occidental than Chinese populations. Therefore aging has a marked effect on aortic morphology in the occidental and Chinese populations influenced by both atherosclerosis and hypertension. These morphologic changes may account for the findings of increased aortic pulse wave velocity observed with advancing age and may be responsible for the systolic hypertension seen in aging populations. (Am J Pathol 1991, 139:1119–1129)

The aorta undergoes marked changes with normal aging: it becomes tortuous because of increase in length, it dilates to the extent that its intimal surface area doubles between the second and sixth decade, and its wall increases in stiffness, leading to an increase in aortic pulse wave velocity.[1–5] These changes are due predominantly to alterations in the structural and physical properties of the arterial wall and are present in normal aging populations. Hypertension and atherosclerosis also occur in aging populations, and their prevalence is known to vary in different racial groups around the world. Reports from the occidental and Chinese population indicate a possibility that differences in the prevalence of atherosclerosis and hypertension may exist with a lower and higher prevalence of atherosclerosis and hypertension, respectively, in the Chinese.[5–8] Thus aging studies in any given population are generally complicated by the concomitant presence of hypertension and atherosclerosis, which in many cases are present but asymptomatic. A wealth of information has been collected in many comparative studies, using populations with known differences of cardiovascular diseases to study the effect of age on specific cardiovascular parameters.[9–13] We previously have examined the age-related changes on arterial distensibility in populations with a high and low prevalence of hypertension by comparing two separate groups in China—a northern urban community in Beijing and a southern rural community in Guangzhou.[6] These studies found that although the prevalence of atherosclerosis in Chinese is lower than that in western populations, the increase in pulse wave velocity with age in the northern community was much higher than that seen in a number of western populations. Pulse wave velocity was also markedly higher than that observed in the southern Chinese community, which had a much lower prevalence of hypertension than the northern community. These studies concluded that hypertension has a greater effect on the age-related increase in aortic pulse wave velocity than does atherosclerosis.

The aim of this investigation was to examine the effects of age on geometric parameters of the aorta and the structural components of the aortic wall in populations with varying degrees of hypertension and atherosclerosis. We attempted to separate the effects of aging from those of hypertension and atherosclerosis. This report is the first stage of the study comparing occidental populations (Americans and Australians) and Oriental populations (China: Beijing, Guangzhou, and Shanghai).

Material and Methods

Tissue Collection

For the present study, human aorta specimens were collected from three different continents: America, Australia, and Asia (China) from five different centers. The Chinese populations were chosen from different regions because of high (Beijing) and low (Guangzhou) prevalence of hypertension, with a low prevalence of atherosclerosis.[8] Shanghai, situated geographically between Beijing and Guangzhou, was included because its population has an intermediate prevalence of hypertension. The American (Baltimore, Maryland) and Australian (Sydney) populations have a high prevalence of atherosclerosis and were compared with the Chinese.

Aortic specimens were collected at autopsy from patients of both sexes, ranging in age from 19 years to more than 65 years, over a 3-year period (March 1987 to February 1990). The specimens were from patients dying from traumatic, accidental, or natural causes (aortas with inflammatory diseases were excluded from the study). A questionnaire was completed by the examining pathologist that documented the circumstance of death, age, race, sex, height, weight, and any known measurement of blood pressure or hypertension (pressures [systolic or diastolic] greater than 140/90 mm Hg, as defined by Framingham were used as a criteria of hypertension).[13]

Fixation and Processing

The total length of the aorta was resected from 1 cm above the aortic valve annulus to just above the bifurcation of the abdominal aorta. A tapered Lucite stopper with a central lumen was inserted into each cut end of the aorta and secured with ligatures on the adventitial surface (Figure 1). All large and small arterial branches were occluded with surgical staples or ligatures, taking care to avoid distortion of the aorta. All vessels were perfusion fixed through the ascending aorta at 100 mm Hg pres-

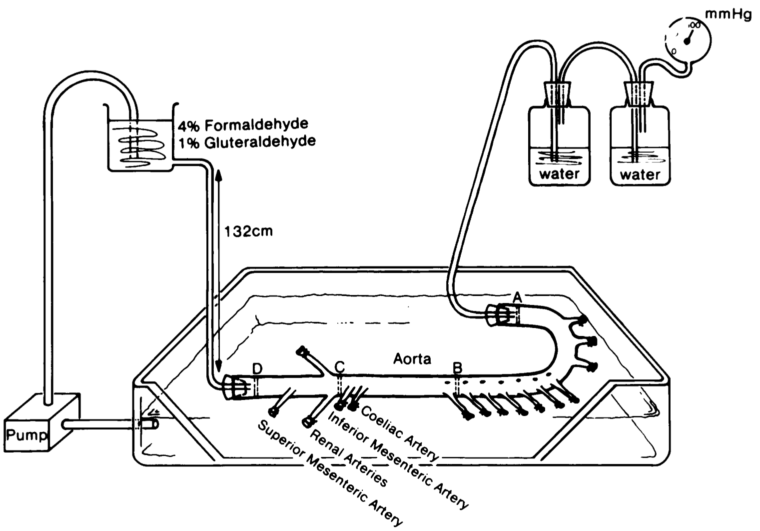

Figure 1. *Method used for perfusion fixation of the aorta with McDowell–Trump solution (4% formaldehyde and 1% glutaraldehyde) and four locations* (A, B, C, D) *from which ring sections of the aorta were taken for histologic examination and morphologic measurements.*

sure using 4% formaldehyde and 1% glutaraldehyde in phosphate buffer (McDowell—Trump fixative[14]) for 60 minutes. This pressure and duration of fixation was chosen because under these conditions the elastic lamellae are straight, and medial smooth muscle contact to elastic fibers occurs at longitudinal ridges associated with peripheral dense bodies.[15] These junctions are distorted at higher pressures. Four 0.5-cm transverse rings of aorta were sampled for morphologic studies: A) ascending aorta 1.5 cm from the proximal end; B) descending thoracic aorta between the sixth and seventh intercostal arteries; C) abdominal aorta just above the renal arteries; and D) abdominal aorta 1.5 cm above the distal cut end of the abdominal aorta. In 16 cases, the aortic circumference was measured at site B at 100 mm Hg pressure with saline and again after fixation with McDowell—Trump fixative, to determine the percentage of circumferential shrinkage due to fixation and later due to dehydration (paraffin embedding and sectioning).

Left and right kidney sections 1.5 × 1.5 × 0.3 cm cut perpendicular to the hilum of the kidney were taken from the cortex and the medulla. The presence of antemortem hypertension was determined by clinical history and further evaluated by the degree of kidney arterial and arteriolosclerosis (see below).

Tissue Processing for Light Microscopy

Sections of the aorta from four locations and two sections from the kidney were processed in a graded series of alcohol and embedded in paraffin. Multiple sections were cut at 6-μ thickness and stained by hematoxylin and eosin (H&E), Weigert-van Gieson elastic stain, Movat pentachrome stain (aortic and kidney sections), and alcian blue-PAS (periodic acid-Schiff) metanil yellow (kidney sections).

Grading of Hypertension

Kidney sections stained by H&E and alcian blue-PAS-metanil yellow[16] were used for quantitating the extent of arterial changes in muscular arteries (150- to 500-μ diameter) as well as arterioles (≤150-μ diameter) by a modified Tracy method.[16–18] The extent of medial wall thickening as well as fibrointimal proliferation was determined, and a score of 1 to 5 was given as follows: no intimal or medial thickening, grade 1; mild focal intimal proliferation such that the endothelial cells are no longer in direct contact with underlying elastin, grade 2; intimal proliferation equal in thickness to the media, grade 3; intimal proliferation resulting in cross-sectional luminal narrowing of 25% to 50%, grade 4; and luminal narrowing greater than 50% by intimal proliferation, grade 5. A minimum of 20 vessels at 100 to 150 times magnification were evaluated. Scores from all vessels 80 to 500 μ in diameter were combined, and the mode of the grades was used as the measurement. Hypertension was considered to be present if the grade was at least 3.

Grading of Atherosclerosis

The extent of aortic atherosclerosis was quantitated histopathologically as follows: grade 1, no atherosclerosis; grade 2, foam cell lesions; grade 3, fibrous plaque consisting of a central pultaceous debris with overlying fibrous cap; and grade 4, complicated lesions consisting of hemorrhage, ulceration, thrombosis, or calcification. All aortic sections were separately given an atherosclerotic score. Group means for ages 19 to 44, 45 to 64, and more than 65 years were derived for each region and age group.

Morphometric Measurements

Sections stained by Weigert-van Gieson elastic stain were projected at ×5 magnification using a Bessler photographic enlarger, and the lumen, the internal elastic lamina, and the medial adventitial borders were traced. The area of lumen, the area within the internal elastic lamina, and the medial adventitial area were determined by planimetry using the software "MORPH" program (Woods Hole Association, Boston, MA). Morphologic areas were used to compute the medial thickness, intimal plaque thickness, and the outer circumference of the aorta (medial adventitial border).

Study Population

Data were obtained from 302 subjects, ranging in age from 19 to 104 years (Table 1). Of these, 80 subjects were from Australia, 110 from China, and 112 from the United States of America. The ratio of male to female was approximately 2 to 1. The patients were grouped into three groups: 19 to 44; 45 to 64; and 65 years and older. This grouping was used because ages 19 to 44 are considered as young adults, 45 to 64 as middle aged, and age 65 years and greater as old age. The cause of death in the occidental population was coronary heart disease, 29%; trauma, 17%; drug overdose, 16%; suicide, 7%; respiratory diseases, 6%; malignant neoplasms, 5%; cerebrovascular accidents, 4%; and miscellaneous causes, 16%. In the Chinese, the cause of death was malignant neoplasms, 20%; respiratory diseases, 19%; coronary heart disease, 15%; cerebrovascular accidents, 11%; renal failure, 10%; sepsis, 6%; gastrointestinal bleeding, 5%; cirrhosis liver, 5%; valvular heart disease, 4%; and miscellaneous causes, 5%. Seventy-one patients (24%) were clinically hypertensive. The highest prevalence of clinical hypertension was in China (34%), the lowest in Australia (4%), and an intermediate prevalence (21%) was found in the United States.

Data were not uniformly available in all cases. Of the 302 subjects studied, kidney samples were available in 269 (Table 1). Two hundred sixty-three aortic samples were measured in the A location, 296 in B, 293 in C, and 284 in D. Samples were omitted only for technical reasons such as difficulty in obtaining ascending aorta (inability to collect samples in location A in Australia from 30 cases and from three in the United States and China), extreme distortion from heavy calcification, or inability to cut sections because of inadequate decalcification, which occurred in three sections in location D; they were not entered into the analysis. The rest of the missing cases had not been stained by Weigert-van Gieson stain.

The populations from the three Chinese cities were combined to obtain adequate numbers for comparison of populations from China and from the western occidental populations (Australia and the United States).

Statistical Analysis

All data for each subject were entered into dBase IV database program. All group data in the text and figures are represented as mean ± standard error of the mean (SEM). The relationships between variables were compared by means of least-squared linear regression anal-

Table 1. *Total Cases Collected During the Study Tabulated for Five Different Populations by Age, Sex, and Age-group Distribution, Number of Patients with Clinical Hypertension, and Total Number of Kidney Sections Examined within Each Group*

		Australia	China			USA
	Total	Sydney	Beijing	Guangzhou	Shanghai	Baltimore
No. of cases	302	80	47	30	33	112
Age mean ± SEM	55 ± 1	63 ± 2	62 ± 3	74 ± 4	67 ± 4	50 ± 2
No. males	206	53	26	12	19	78
No. females	127	27	21	18	14	34
Age group			number (Mean ± SEM)			
19–44	85 (32 ± 2)	18 (33 ± 2)	9 (34 ± 3)	3 (34 ± 5)	6 (31 ± 3)	49 (34 ± 1)
45–64	87 (56 ± 1)	22 (55 ± 1)	15 (57 ± 2)	6 (53 ± 3)	3 (57 ± 4)	41 (56 ± 1)
≥65	130 (79 ± 2)	40 (80 ± 1)	23 (77 ± 2)	21 (85 ± 2)	24 (77 ± 2)	22 (77 ± 2)
No. patients with H/O hypertension*	71	3	16	13	14	25
No. of cases w/kidney analysis	269	76	47	21	31	94

* Hypertension data relate only to subjects in whom information is available.
H/O = history of.

ysis. The analysis was performed using a general linear models procedure (Statistical Analysis System, SAS Institute, Cary, NC). Each variable was adjusted for the covariates age, height, and weight. After adjusting for these variables, the main effect of hypertension (as determined by kidney changes), sex, and country were tested along with the interaction term of hypertension by country.

Results

Autopsy Data Regarding Height, Body Weight, and Heart Weight in Five Populations Greater than 18 Years of Age

The American and Australian populations were similar in height, weight, and heart weight (Table 2). In the three regions of China, the height was similar, but body and heart weight were significantly less in the group from Guangzhou compared with that of Beijing ($P = 0.02$) after adjusting for age, height, and weight.

Morphometric Measurements

Circumference of the Aorta

A progressive decrease in aortic circumference (Figure 2) occurred from sites A to D (thoracic to abdominal aorta) in all populations and age groups. Also aortic circumference increased with age in all populations and regions, with the largest increase in circumference seen in the ascending aorta (A) and the smallest in the abdominal aorta (D) (Figure 2). The Chinese had a larger aortic circumference in site A (9.33 ± 0.26 cm) in the age group more than 65 years of age (Figure 2) than the occidental population (8.74 ± .21). In locations B, C, and D, however, the occidental population had a larger circumference in all age groups. The Chinese showed a constant proportional enlargement of the aorta at all locations; the United States and Australia showed a significantly greater ($P = 0.04$) proportional growth of the abdominal than of the thoracic segment (Figure 2).

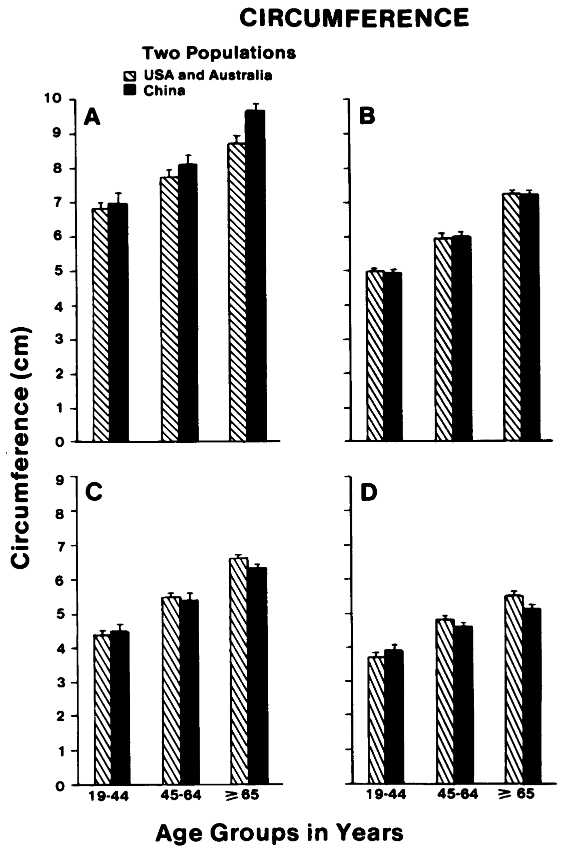

Figure 2. *Mean and SEM of the aortic circumference (cm) at four different locations* (A, B, C, D) *in the aorta by three age groups: 19 to 44 years; 45 to 64 years; ≥65 years in two populations, occidental (USA and Australia) and Chinese.*

Medial Thickness of the Aorta

A similar progressive decrease in the medial thickness (Figure 3) occurred from ascending thoracic aorta to abdominal aorta in all populations and in all age groups. The medial thickness did not change significantly with age in any population; however, only in position D there appeared to be a trend toward medial thinning with age.

Table 2. *Autopsy Data of Height, Body Weight, and Heart Weight (Adjusted for Age, Height, and Weight) in Five Populations (mean ± SEM)*

Population	n	Age (yr)	No. w/hypertension	Ht (cm)	Wt (kg)	n	Heart Wt (g)
USA	111	50 ± 2	38	171 ± 1	77 ± 25	93	395 ± 11
Australia	80	62 ± 2	34	167 ± 1	65 ± 20	73	396 ± 11
Chinese							
Beijing	47	62 ± 3	26	159 ± 1	56 ± 13	46	400 ± 14
Shanghai	33	67 ± 4	23	160 ± 2	54 ± 10	30	367 ± 22
Guangzhou	29	74 ± 4	14	158 ± 3	44 ± 13	20	346 ± 19*

* $P = 0.02$, comparing heart weight of individuals from Guangzhou with Beijing, USA, and Australia.

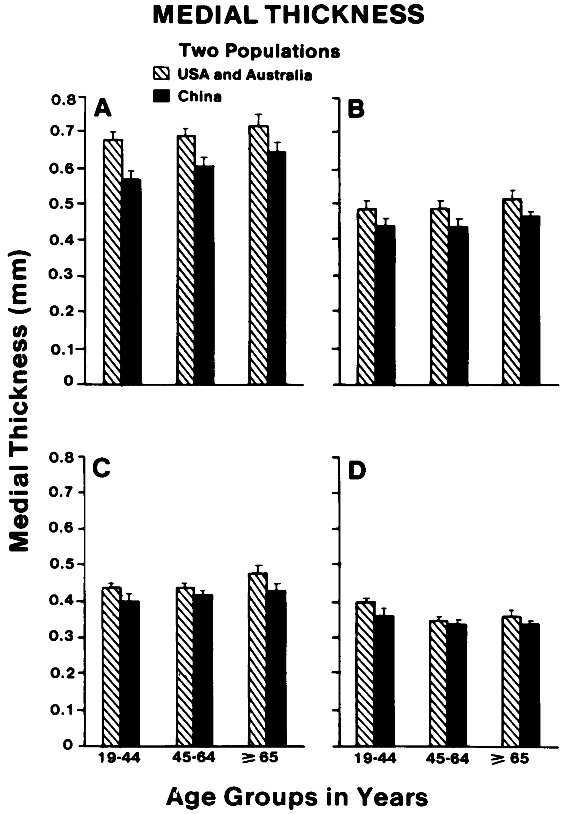

Figure 3. *Mean and SEM of the aortic medial thickness (mm) at four different locations* (A, B, C, D) *in the aorta by three age groups in two populations.*

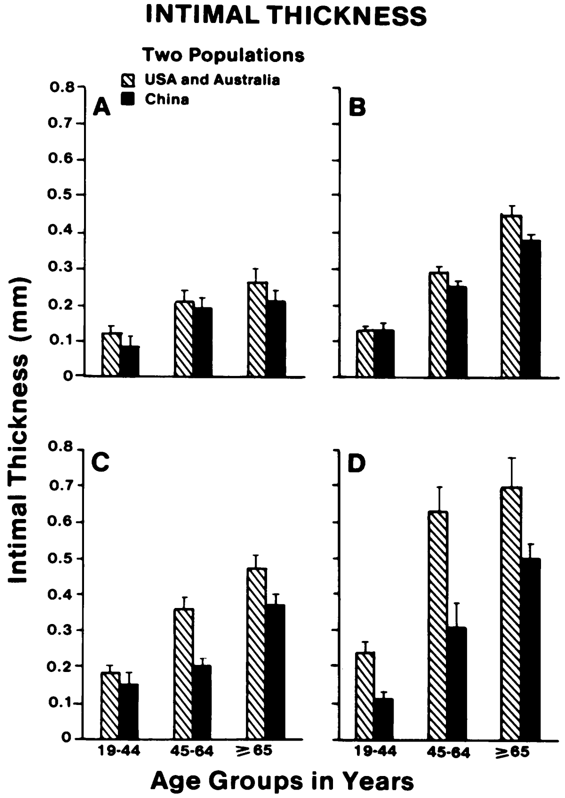

Figure 4. *Mean and SEM of the aortic intimal thickness (mm) in four different locations* (A, B, C, D) *in the aorta by three age groups in two populations.*

Intimal Thickness

Intimal thickness (Figure 4) increased with advancing age in all populations and was maximal in abdominal aorta. The differences in the occidental and Chinese population was dramatic in the 45 to 64 and the over 65 age groups in the abdominal aorta (C and D), with the greatest intimal thickness (secondary to atherosclerosis) occurring in the occidental population. In the ascending and descending thoracic aorta (A and B), the intimal thickness also increased with age and was greater in the occidental than the Chinese population, but the differences were not as marked (Figure 4).

Progression of Atherosclerosis by a Semiquantitative Scoring Scheme

The stage of atherosclerosis (Figure 5) increased similarly in both the occidental and Chinese populations with increasing age, and was most predominant in the distal abdominal aorta. The grade of atherosclerosis was similar in the occidental and Chinese for the 19- to 44-year age groups in all locations; however, the occidental population had a higher grade of atherosclerosis in the abdominal aorta (C and D) in the 45- to 64-year and the over 65-year age groups.

Correlation of Kidney Histologic Changes with Clinical History of Hypertension

Of the 269 cases evaluated, 133 showed either no change or only mild intimal thickening of the arteries and arterioles and were considered normal, whereas 136 showed arterial changes ranging from grade 3 to grade 5, which were indicative of clinical hypertension. The prevalence of hypertension was the highest in Shanghai (74%) by morphologic criteria also; nearly 77% of the population was more than 65 years of age. Beijing had the second highest prevalence (55%), with only 49% of the population older than 65 years. Guangzhou had the lowest prevalence of hypertension (47%), with 70% of the population under the age of 65 years. The prevalence of morphologic hypertension in the Americans and Australians was lower (40% and 45%), with 23% and 53% of the population aged more than 65 years. Because the prevalence of clinical hypertension was highest in the Chinese, this population was used to determine the sensitivity and specificity for this method of analysis. The sensi-

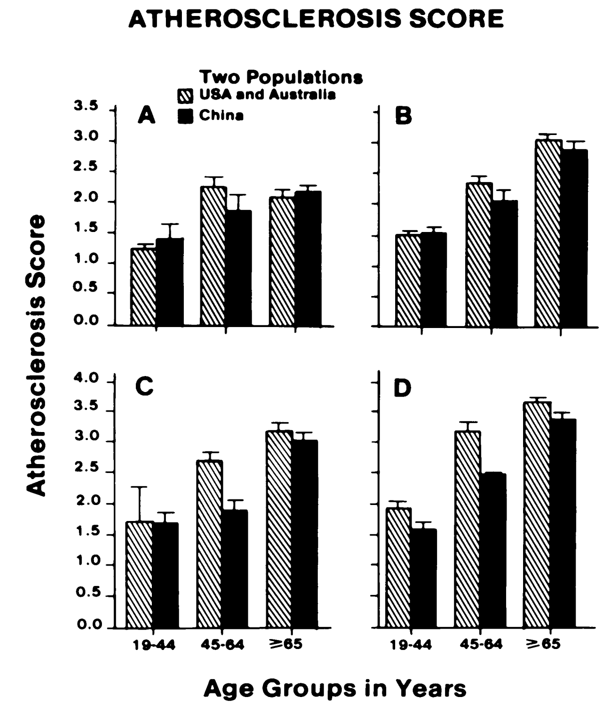

Figure 5. *Mean and SEM of the aortic atherosclerosis score determined by histologic assessment of intima: 1 = no atherosclerosis; 2 = foam-cell lesions; 3 = fibrous plaque; and 4 = complicated plaque in four different locations* (A, B, C, D) *in the aorta in three age groups in two populations.*

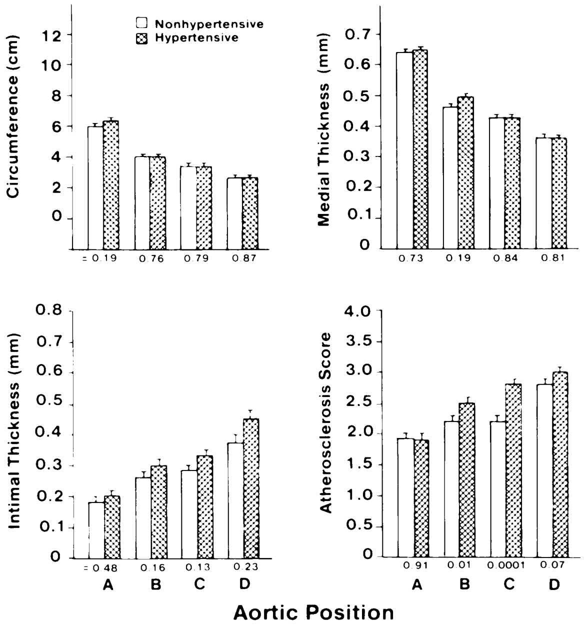

Figure 6. *Effect of hypertension as determined by kidney changes on aortic circumference, medial thickening, intimal thickening, and atherosclerosis score in all populations greater than 18 years of age after adjusting for the effects of age, height, and weight.*

tivity was 76%, specificity 58%, the calculated predictive value of a positive test was 81%, and the predictive value of a negative test was 50%. (In the elderly patients, caution must be exercised because renal arterial changes may occur as a consequence of aging and may not be from hypertension alone).

Effect of Hypertension Determined by Kidney Changes, Sex, and Country Were Tested Along with the Interaction of Hypertension by Country After Adjusting for Age, Height, and Weight

Figure 6 shows the effect of hypertension on aortic circumference, medial thickness, intimal thickening, and atherosclerosis score in all populations after adjusting for age, height, and weight. Significant differences were seen only for atherosclerosis score, with hypertensives having a higher score in locations B, C, and D. Effect of hypertension on the aortic circumference was compared by country (Figure 7), after adjusting for age, height, and weight; the response to hypertension was different in the Chinese: in location A there was dilation, whereas in locations B, C, and D a decrease in aortic circumference was noted in hypertensives; the occidental population showed no effect in A but a dilation in B, C, and D with hypertension; these different responses were significantly different in location D (Table 3). Also after adjusting for age, height, and weight, the presence of hypertension resulted in significantly greater heart weights. Men had greater heart weights than women, and the occidental population had greater heart weights than the Chinese population (Figure 8). The effects of country on aortic circumference after adjusting for age, height, and weight were also compared. The aortic circumference was significantly larger in the Chinese compared with the occidental in position A (Figure 9). However, intimal thickening and atherosclerosis scores were significantly greater in the occidentals than the Chinese population in locations B, C, and D for the former and D for the latter (Figure 9 and Table 3). Surprisingly the media was significantly thicker in the occidental than in the Chinese locations A and C.

Effects of Fixation and Embedding

Sixteen aortic specimens were perfused at 100 mm Hg with saline, and their lengths and circumferences were measured. This value was compared with that obtained after 60 subsequent minutes of perfusion with McDowell-Trump fixative. The retraction in length (a result of fixation) was 5.8% (SEM 1.0), whereas the circumferential retraction was 6.5% (SEM 0.9) and was age dependent (slope = -0.19; $r = 0.76$, $P < 0.001$). The circumferential measurement in aortae before and after paraffin em-

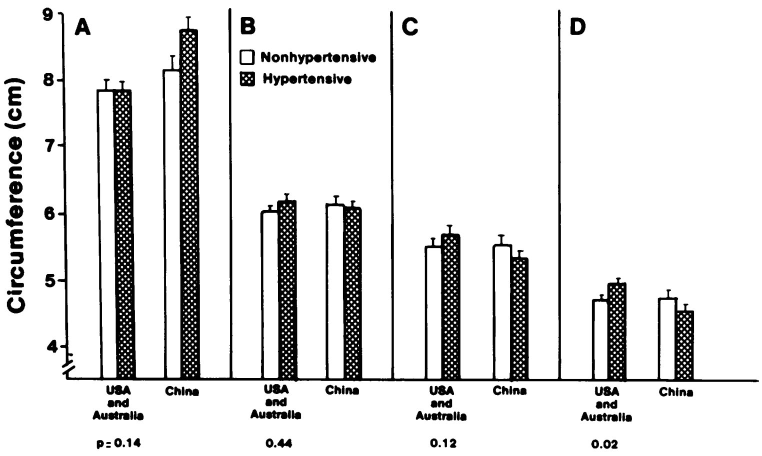

Figure 7. *Mean and SEM of the effect of hypertension on the aortic circumference in the occidental and Chinese population after adjusting for the effect of age, height, and weight. Note significant difference in the* (D) *position between the occidental and the Chinese population (*P *= 0.02).*

bedding also showed a reduction of 18.9 ± 5.4%. The measurement of wall thickness in these aortae before and after paraffin embedding showed a reduction of 18.1 ± 2.5%. This shrinkage was greatest in the abdominal aorta as compared with the ascending aorta, but was not statistically significant. Because all tissue was processed in a similar manner, it was deemed unnecessary to allow for these effects when comparing measurements among similar age groups.

Discussion

One of the most striking features of aging on the human aorta is the change in its physical properties. The amplitude of pressure wave progressively increases with increasing age, with a concomitant increase in pulse wave velocity.[4–6] Morphologic studies that investigate the structural bases for these findings are complicated by hypertension and by atherosclerosis-induced changes. The present study addresses these issues and further correlates the aging changes in various populations and attempts to separate the effects of aging from those of hypertension and atherosclerosis.

Our study demonstrates that aortic circumference increases with age and is maximal in the ascending aorta and minimal in the abdominal aorta, especially when the effects of height and weight are taken into account. Age appears to have minimal effect on medial thickness, whereas the effect on intimal thickness is pronounced. The increase in intimal thickness with age is the predominant factor for the well-known age-related increase in total wall thickness of the aorta.[19–21] That intimal thickness is maximal in the abdominal aorta as compared with other locations is a well-known effect of atherosclerosis. The clear relationship between increase in intimal thickness and the progression of atherosclerosis indicates that the semiquantitative method for grading the atherosclerosis is a useful method for the overall evaluation of the presence of intimal thickness. A greater differential effect is seen in the Chinese population, however, which shows a far smaller effect of age because of a low prevalence of atherosclerosis in this population. Differences between occidental and the Chinese populations were seen in the circumference, medial thickness, intimal thickness, and atherosclerosis score at various locations in the aorta. There is a significantly greater circumference of the ascending aorta in the Chinese than in the occi-

Table 3. *Relationship of Hypertension, Country, and Interaction of Hypertension by Country Adjusted for Age, Height, and Weight (see Figure 9) Using General Linear Models Procedure*

	P value			
	A	B	C	D
Source		Circumference		
Hypertension	0.195	0.759	0.789	0.873
Country	0.008*	0.883	0.198	0.134
Country hypertension	0.140	0.442	0.121	0.024†
		Intimal thickness		
Hypertension	0.484	0.164	0.126	0.229
Country	0.794	0.023‡	0.010‡	0.005‡
Country hypertension	0.702	0.199	0.728	0.812

* China > USA and Australia = 8.4 > 7.9.
† China: nonhypertensive vs. hypertensive 4.9 > 4.5; USA and Australia: 4.5 < 4.7.
‡ USA and Australia > China: 0.30 > 0.25; 0.35 > 0.26; and 0.50 > 0.33.

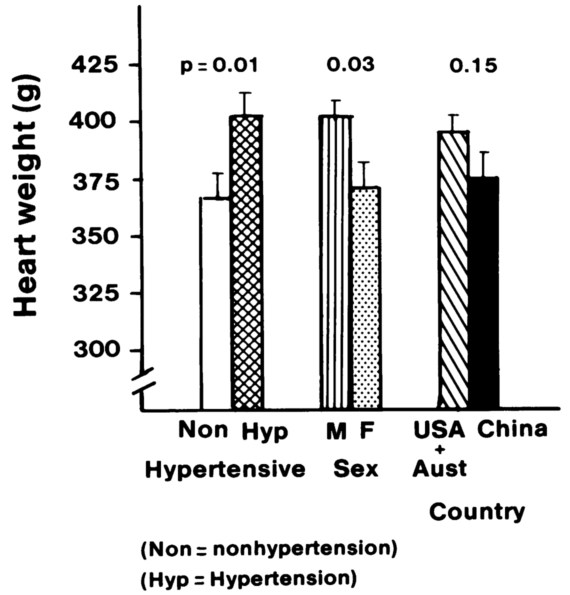

Figure 8. *Mean and SEM of the effect of hypertension, sex, and country of origin on heart weight after adjusting for age, height, and weight.*

dental. This tendency is reversed, however, progressing down to the abdominal aorta. Also the Chinese showed a constant proportional enlargement of the aorta in all locations with age, but the occidental population had a significantly greater growth of the abdominal aorta than of the thoracic aorta. One explanation for this difference has been attributed to the higher prevalence of atherosclerosis in the occidental population; its effects are most marked in the abdominal aorta because of atherosclerosis-induced medial destruction with resultant aortic dilation.[22–25] Our study does not corroborate this, however, because the occidental population had a significantly thicker abdominal aortic wall than the Chinese. Atherosclerotic destruction of the media in the past has been given as an explanation for the high prevalence of abdominal aneurysms seen in patients with advanced atherosclerotic disease.[26] Our study suggests a decrease in tensile strength as age advances rather than atherosclerosis alone being a contributor to the formation of abdominal aortic aneurysms.

The effects of hypertension also were addressed in this study. There appears to be an independent contribution from hypertension to the age-related increase in aortic circumference and intimal thickness. An appearance of increased aortic circumference is seen in hypertensives only among occidentals at locations B, C, and D, and among Chinese at location A; a paradoxically small circumference is seen in hypertensive Chinese at locations B, C, and D, and the population differences are statistically significant at location D (Figure 7). These results indicate that hypertension may be related differently to aortic dimensions in occidental and Chinese populations.

In all populations, we relied on morphologic changes in the renal vessel for a judgment of hypertension. Tracy

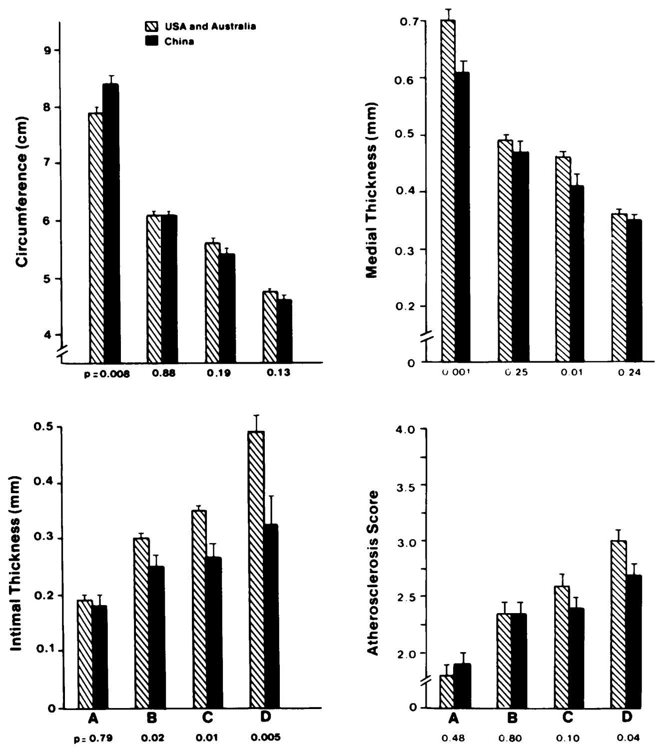

Figure 9. *Mean and SEM of the effect of country of origin (occidentals versus Chinese) on the aortic circumference, medial thickness, intimal thickness, and atherosclerosis score after adjusting for age, height, and weight. Note significantly larger aortic circumference in* (A) *in the Chinese and significantly greater medical thickness in* (A) *and* (C) *intimal thickening in* (B), (C), *and* (D) *and atherosclerosis in* (B), (C) *and* (D) *locations in the occidental population.*

and co-workers have previously shown the effects of hypertension on small vessels within the kidney (50 to 300 μ).[16–18] Kidney arterioles and arteries undergo medial and intimal thickening with normal aging, but these changes are accelerated in the presence of hypertension. Therefore the presence of hypertension may be determined by quantitative morphologic parameters of the renal arterioles and arteries. Tracy has shown an excellent correlation of clinical hypertension with kidney arterial changes in autopsies of several defined population groups with multiple blood pressure recordings before their natural deaths.[17] Our own results in the Chinese populations have shown that a semiquantitation morphologic grading scheme of kidney arterial changes correlates well with clinical hypertension. For correlation of our histopathologic grading scheme, we limited our study to the Chinese population, as the blood pressure measurements were clinically documented and the prevalence of clinical hypertension has been documented previously to be the highest in this population.[5–8]

This study indicates that the observed increase in atherosclerosis score in hypertensives was statistically significant in locations B, C, and D after adjusting for age, height, and weight, yet intimal thickness as a whole failed to show a significant difference between hypertensives and nonhypertensives. This suggests that hypertension may increase necrotic cores of atherosclerosis, but otherwise may have no impact on intimal thickness. The differential effects of hypertension on the occidental and Chinese populations on aortic circumference were only significant in the D location. As more data become available, however, similar analysis will be carried out to separate the effects of aging from those of hypertension on both functional and structural aortic parameters, especially in the Chinese, where prevalence of hypertension is markedly different in the northern (Beijing) and southern (Gangzhou) communities.

From these observations, we can conclude that aging has a marked effect on the aortic trunk. Hypertension and atherosclerosis modify this effect, however, so as to cause disproportional changes in circumference, medial thickness, and intimal thickness at different anatomic locations. It is well known that the functional properties and structural composition of the aortic wall change with age.[19–22,27–29] Aging results in the loss of elasticity and a parallel increase in collagen and mucopolysaccharide.[28,29] Also it has been speculated that smooth muscle cells undergo degeneration with age and realignment. The mechanisms for loss of elastic recoil have not been established. Whether this is the result of loss or fragmentation of elastic lamella or due to modifications of interlamellar connections through elastic fibers or smooth muscle cells that anchor the elastic lamellae[30–33] remains unknown. Explanation for our observations in these populations will require detailed study of the aortic wall components, ie, elastic fibers, smooth muscle cells, collagen, and mucopolysaccharides. Preliminary results from other laboratories of scanning electron microscopic studies on digested aortic samples have shown a decrease in interlamellar elastic fibers in hypertensive patients as well as in patients with aortic dissecting aneurysms.[34] This implies that the mechanisms responsible for aortic dissection may be related to hypertension in many cases. To increase our understanding of the relationship of aging and hypertension in populations with known differences in prevalences of hypertension and atherosclerotic diseases, detailed morphologic techniques will be carried out in future studies.

References

1. Cliff WJ: Aging in the arterial wall, Interdis Topics Gerontol Vol 11. Edited by HP van Haher. Basel, Karger, 1977, pp 89–99
2. Meyer WW, Walsh SZ, Lind J: Functional morphology of human arteries during fetal and postnatal development, Structure and Function of the Circulation. Vol 1. Edited by CJ Schwartz, NT Werthessen, S Wolf. New York, Plenum Press, 1980, pp 95–379
3. Mitchell JRA, Schwarts CJ: Arterial Disease. Oxford, Blackwell Scientific Publications, 1965
4. O'Rourke MF. Arterial Function in Health and Disease. London, Churchill Livingstone, 1982
5. Avolio AP, Chen SG, Wang RP, Zhan CL, Li MF, O'Rouke MF: Effects of ageing on changing arterial compliance and left ventricular load in a northern Chinese urban community. Circulation 1983, 68(1):50–58
6. Avolio AP, Deng FQ, Li WQ, Luo YF, Huang Zo, Xing LF, O'Rourke M: Effects of aging on arterial distensibility in populations with high an low prevalence of hypertension: Comparison between urban and rural communities in China. Circulation 1985, 71(2):202–221
7. Liu CK: Cardiovascular diseases in China. Am J Cardiol 1962, 10:367–370
8. Wu YK, Yu JS, Gao RQ, Lu CQ, He GQ, Yu MC: Epidemiology and community control of hypertension, stroke and coronary heart disease in China. Chung Kuo I Hsueh Ko Hsueh Yuan Hsuch Pao 1979, 1:1–6
9. Restrepo C, Malcolm GT, Strong JP, Toca UT, Tracy DE: Microscopic morphometry of abdominal aorta from men in New Orleans and Guatemala. Arteriosclerosis 1982, 2:242–251
10. Nakashima T, Tanikawa J: A study of human aortic distensibility with relation to atherosclerosis and ageing. Angiology 1971, 22:477–490
11. Gore I, Nakashima T, Imai T, White PB: Coronary atherosclerosis and myocardial infarction in Kyushu, Japan and Boston, Massachusetts. Am J Cardiol 1962, 10:400–406
12. Kesteloot H, Lee CS, Park HM, Kegels C, Geboers J, Claes

JH, Jossens JV: A comparative study of serum lipids between Belgium and Korea. Circulation 1982, 65:795–799

13. Kannel WB, Sorlie P: Hypertension in Framingham, Epidemiology and Control of Hypertension. Edited by O Paul. Miami, Symposia Specialist, 1975, p 533
14. McDowell EM, Trump BF: Histologic fixatives suitable for diagnostic light and electron microscopy. Arch Pathol Lab Med 1976, 100:405–414
15. Clark JM, Glagov S: Structural integration of the arterial wall: I. Relationships and attachments of smooth muscle cells in normally distended and hyperdistended aortas. Lab Invest 1979, 40:587–602
16. Tracy RE, Johnson WD, Lopez CR, Toca BT: Hypertension and arteriosclerosis of the kidney, pancreas, adrenal gland, and liver. Virchows Arch [A] 1981, 391:91–106
17. Tracy RE, Tabares TV. Nephrosclerosis and blood pressure: I. Rising and falling patterns in lengthy records. Lab Invest 1974, 30:20–29
18. Tracy RE, Duran MV, Heigle T, Oalmann MC: Two variants of nephrosclerosis separately related to age and blood pressure. Am J Pathol 1988, 131:2:270–282
19. Gozna ER, Shaw AEM, Holland JG: Age-related changes in the mechanics of the aorta and pulmonary arteries of man. J Appl Physiol 1974, 36:407–411
20. Toda T, Tsuda N, Nishimori I, Leszcznski DE, Kummerow FA: Morphometric analysis of the aging process in human arteries and aorta. Acta Anat 1980, 106:35–44
21. Goyal VK: Changes with age in the aorta of man and mouse. Experimental Gerontology 1982, 17:127–132
22. Movat HZ, More RH, Haust DM: The diffuse intimal thickening of the human aorta with aging. Am J Pathol 1958, 34:1023–1031
23. McGill HC Jr, Sandler M, Bourne GH: Natural history of human atherosclerotic lesion, Atherosclerosis and Its Origin. Edited by M Sandler, GH Bourne. New York, Academic Press, 1963, p 42
24. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ: Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987, 316:1371–1375
25. Zarins CK, Weisenberg E, Kolettis G, Ku, DN, Glagov S: Differential enlargement of artery segments in response to enlarging atherosclerotic plaques. J Vasc Surg 1988, 7:386–394
26. Eagle AE, DeSanctis RW. Diseases of the aorta, Heart Disease. A Text Book of Cardiovascular Medicine. Edited by E Braunwald. Philadelphia, WB Saunders, 1988, p 1542
27. Spina M, Garbisa S, Hinnie J, Hunter JC, Serafini-Fracassini A: Age-related changes in composition and mechanical properties of the tunica media of the upper thoracic human aorta. Atherosclerosis 1983, 3:64–76
28. Hosoda Y, Kawano K, Yamasawa F, Ishii T, Shibata T, Inayama S: Age-dependent changes of collagen and elastin content in human aorta and pulmonary artery. Angiology 1984, 35:615–621
29. Schlatmann TJM, Becker AE: Histologic changes in normal aging aorta. Implications for dissecting aortic aneurysms. Am J Cardiol 1977, 39:13–20
30. Wolinsky H, Glagov S: Comparison of abdominal and thoracic aortic medial structure in mammals. Deviation of man from the usual pattern. Circ Res 1969, 26:677–686
31. Wolinsky H, Glagov S: A lamellar unit of aortic medial structure and function in mammals. Circ Res 1967, 20:99–111
32. Clark JM, Glagov S: Transmural organization of the arterial media. The lamellar unit revisited. Atherosclerosis 1985, 5:19–34
33. Dingmans KP, Jansen N, Becker AE: Ultrastructure of the normal human aortic media. Virchows Arch 1981, 392:199–216
34. Nakashima Y, Shiokawa Y, Sueishi K: Alterations of elastic architecture in human aortic dissecting aneurysm. Lab Invest 1990, 62:751–760