Hypertension is an independent risk factor for coronary artery disease and carotid and lower extremity occlusive disease. Other multivariate clinical studies have shown that pulse pressure is also an independent risk factor for atherosclerosis. Previous experimental studies in our laboratory and in others have demonstrated that surgically created aortic coarctations increase blood pressure proximal to the coarctation and increase the rate of plaque deposition in hypercholesterolemic rabbits and monkeys.

On the other hand, the aorta distal to a severe coarctation experiences reduced wall motion and is largely protected from plaque formation despite hypercholesterolemia in animals. In a separate study, rigid external casts of lesion-prone arteries in normotensive hypercholesterolemic rabbits inhibited plaque formation, perhaps because of reduced wall motion. In the present experiment, we reduced aortic wall motion in the hypertensive atherosclerosis-prone aorta proximal to a coarctation by externally wrapping a segment of aorta and studied the effect on plaque formation.

**Key Words:** wall motion ▪ hypertension ▪ atherosclerosis ▪ pulse pressure

**Methods**

Twenty-six adult male New Zealand White rabbits weighing 2.5 to 3.5 kg were fed an atherogenic diet consisting of 1% cholesterol and 4% corn oil in standard rabbit chow. Twenty rabbits underwent tight thoracic aortic banding, and 6 rabbits underwent aortic banding without aortic constriction. A polytetrafluoroethylene (PTFE) external wrap was placed in 13 rabbits. The rabbits were fed the atherogenic diet for 3 weeks. Four groups were studied: 1, coarctation control (no wrap, n = 7); 2, coarctation with loose wrap (n = 6); 3, coarctation with firm wrap (n = 7); and 4, control (noncoarcted, n = 6). Wall motion, blood pressure, and pulse pressure were measured at standard reference sites proximal and distal to the coarctation by use of intravascular ultrasound. Quantitative morphometry was used to measure intimal plaque. Mean arterial pressure and cyclic aortic wall motion were equally increased proximal to the aortic coarctation in all 3 coarcted rabbit groups compared with the control group (P < 0.001). Wall motion in the segment of aorta under the loose and firm wraps was no different from the control value. The external wrap significantly reduced intimal thickening in the 4 groups by the following amounts: group 1, 0.30 ± 0.03 mm²; group 2, 0.06 ± 0.02 mm²; group 3, 0.04 ± 0.02 mm²; and group 4, 0.01 ± 0.01 mm² (P < 0.001). Localized inhibition of aortic wall motion in the lesion-prone hypertensive aorta resulted in significant reduction in intimal plaque formation. These data suggest that arterial wall cyclic motion may stimulate cellular proliferation and lipid uptake in experimental atherosclerosis. (Arterioscler Thromb Vasc Biol. 2000;20:2127-2133.)
In 13 of the 20 coarcted rabbits, the descending thoracic aorta 2 to 3 cm proximal to the coarctation was mobilized and encircled with a 1.5-cm-long segment of PTFE (Figure 1). The PTFE was sutured to itself with horizontal mattress sutures to create a loose (n=6) or firm (n=7) wrap to limit wall motion. The firmness of the wrap was practiced in vivo under intravascular ultrasound guidance to determine the appropriate amount of tension on sutures and to avoid constriction of the aorta.

All animals were begun on an atherogenic diet, consisting of 1% cholesterol and 4% corn oil, 1 day after their thoracotomy, and the diet was continued for 3 weeks. Serum cholesterol was measured before diet induction and at euthanasia. After 3 weeks, the rabbits were sedated with ketamine (40 mg/kg) and xylazine (4 mg/kg), and sedation was maintained with an intravenous mixture of ketamine and xylazine. A catheter was introduced into the femoral artery, and a 5F introducer sheath was placed into the carotid artery. A pediatric pulmonary artery catheter was used under fluoroscopic guidance to advance the carotid sheath into the proximal aspect of the descending thoracic aorta. Blood pressure was simultaneously monitored through the sheath and through the separate femoral artery catheter.

A 30-MHz coronary intravascular ultrasound catheter was introduced through the sheath into the thoracic aorta. A CVIS model 1500-0 ultrasound system (Cardiovascular Imaging Systems, Inc) with a VHS tape recorder was used to perform aortic wall motion studies (Figure 2). Wall motion was recorded at predetermined standard reference points proximal to the coarctation under fluoroscopic guidance. The intravascular ultrasound catheter was then removed and advanced through the femoral artery to the distal thoracic aorta to record wall motion distal to the coarctation.

Aortic wall motion was recorded at standard locations in all 26 rabbits (Figure 1). The locations are depicted in Figure 1A and are defined as follows: level A, proximal aorta (4 cm proximal to the coarctation); level B, wrap segment (2 cm proximal to the coarctation); level C, 2 cm distal to the coarctation; and level D, abdominal aorta at renal artery level. B, Intraoperative photograph at time of placement of the coarctation (plastic clear cable tie, white arrowhead) and PTFE external wrap (black arrowhead). On the left is the firm wrap; on the right, loose wrap.

Aortic wall motion was recorded at standard locations in all 26 rabbits (Figure 1). The locations are depicted in Figure 1A and are defined as follows: level A, proximal aorta (4 cm proximal to the coarctation); level B, wrap segment (2 cm proximal to the coarctation); level C, distal aorta (2 cm distal to the coarctation); and level D, the abdominal aorta (at the level of the renal arteries). Aortic wall cross-sectional area and its changing pulsatile dimensions were recorded for 10 seconds at 25 frames per second at each location. The images were stored on a Macintosh computer, and a commercial program (TapeMeasure, Signa Inc) was used to calculate cross-sectional luminal area at each location. Wall motion (%) is defined as follows: wall motion=(maximum luminal area−minimum luminal area)/(minimum luminal area)×100. Stenosis (%) of the aorta is calculated as follows: stenosis=100×(area of coarctation/diastolic area

Figure 1. A, Diagrammatic representation of thoracic aorta with creation of coarctation by aortic banding. Hypertension and increased atherosclerosis are present proximal to aortic band. External PTFE wrap was placed 2 cm proximal to coarctation to reduce wall motion. Wall motion and intimal cross-sectional area were measured at levels A through D: level A, proximal aorta, 4 cm proximal to coarctation or 2 cm proximal to wrap; level B, wrap level, 2 cm proximal to coarctation; level C, 2 cm distal to coarctation; and level D, abdominal aorta at renal artery level. B, Intraoperative photograph at time of placement of the coarctation (plastic clear cable tie, white arrowhead) and PTFE external wrap (black arrowhead). On the left is the firm wrap; on the right, loose wrap.

Figure 2. Intravascular ultrasound of rabbit aorta at different levels. Wall motion was measured by measuring contours of aortic lumen during cardiac cycle. A, Firm wrap. B, Loose wrap. C, Coarctation. D, Distal thoracic aorta. The aorta is indistinguishable from the firm wrap but is distinguishable from the loose wrap. Wall motion was significantly reduced by the loose and firm wraps. The cable tie significantly reduced aortic area, and distal to the coarctation, poststenotic dilatation is present.
of aorta at the wrap level]. Because the aorta decreases in size the more distal the aorta is from the heart, it would be expected that the stenosis percentage may be slightly overestimated.

The animals were euthanized with intravenous sodium pentobarbital (150 mg/kg). The aortas were immediately excised, and closed aortic rings at levels A through D were sectioned. Light microscopic sections were prepared from the closed aortic rings and were stained with hematoxylin. The intimal and medial areas were calculated by using a commercial computer-controlled digitized tracer (Microcomp Image Analysis, Southern Micro Instruments). Area calculations were determined by tracing contours of the lumen, inner media, and outer media.

All protocols were approved by the Administrative Panel on Laboratory Animal Care at Stanford University, and these studies were performed in accordance with the recommendations of the American Association for the Accreditation of Laboratory Animal Care.

Statistics
Results are expressed as mean±SEM. Statistical analysis was performed by 1-way ANOVA with Student-Newman-Keuls as a post hoc test. Significance was set at a value of P<0.05.

**Results**

**Diet**
Before institution of the atherogenic diet, the mean serum cholesterol level in the 26 rabbits was 29±3 mg/dL. After the diet, the serum cholesterol level increased to 1349±89 mg/dL at 3 weeks (P<0.001). There was no difference in cholesterol level among the 4 rabbit groups. All rabbits maintained a stable weight during the study period.

**Hemodynamic Data**
After 3 weeks, just before euthanasia, mean arterial pressure in the proximal aorta of the coarcted animals (n=20) was increased 40% (90±3 mm Hg) compared with that of noncoarcted control animals (65±3 mm Hg, n=6; P<0.001). Pulse pressure in the proximal aorta of the coarcted animals (43±3 mm Hg) increased >2-fold compared with that of noncoarcted control animals (18±1 mm Hg, P<0.001). Coarctated rabbits had a mean aortic gradient of 20±2 mm Hg (Table 1). Coarctation did not result in any significant change in heart rate. The external aortic wrap did not alter the hemodynamic response to coarctation, and there was no significant difference among the 3 coarcted study groups (Table 2).

Mean blood pressure distal to the coarctation (70±2 mm Hg, n=20) was different from the noncoarcted control value (65±3 mm Hg, n=6). However, pulse pressure was reduced by one half distal to the coarctation (13±2 mm Hg) compared with the noncoarcted control value (23±3 mm Hg, P<0.03).

Cross-sectional aortic dimensions were measured in distal aorta from ultrasound images. There was no difference in cross-sectional area of the proximal aorta between the coarcted and noncoarcted animals. Neither the loose nor the firm wrap resulted in significant narrowing of the aortic lumen cross-sectional area compared with the unwarped or noncoarcted control values (Table 2). The cross-sectional area of the coarctation channel was 4.5±0 mm² and was markedly smaller than the noncoarcted aortic luminal area (24±3 mm², P<0.001). The calculated degree of stenosis was 80% to 83% in the 3 coarcted rabbit groups, with no difference among the groups (Table 2).

**Wall Motion**
The cyclic variation (systolic minus diastolic) of aortic luminal cross-sectional area of the proximal aorta was increased by 70% in the coarcted animals (29±2%) compared with the noncoarcted control animals (17±1%, P<0.001). There was no significant change in aortic wall motion in the thoracic aorta distal to the coarctation. Wall motion in the

### Table 1. Hemodynamic Parameters

<table>
<thead>
<tr>
<th>Coarctation</th>
<th>Proximal MAP, mm Hg</th>
<th>Distal MAP, mm Hg</th>
<th>Gradient MAP, mm Hg</th>
<th>Proximal PP, mm Hg</th>
<th>Distal PP, mm Hg</th>
<th>Heart Rate, bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>No wrap (n=6)</td>
<td>89±4</td>
<td>70±2</td>
<td>19±4</td>
<td>37±3</td>
<td>10±1†</td>
<td>178±4</td>
</tr>
<tr>
<td>Loose wrap (n=6)</td>
<td>89±5</td>
<td>67±5</td>
<td>21±5</td>
<td>48±9</td>
<td>16±4</td>
<td>186±9</td>
</tr>
<tr>
<td>Firm wrap (n=7)</td>
<td>93±2</td>
<td>73±4</td>
<td>20±3</td>
<td>45±3</td>
<td>12±2†</td>
<td>202±13</td>
</tr>
<tr>
<td>Control (n=6)</td>
<td>65±3*</td>
<td>65±3</td>
<td>-0.5±1*</td>
<td>18±1*</td>
<td>23±2</td>
<td>178±7</td>
</tr>
<tr>
<td>Combined coarctation (n=20)</td>
<td>90±3*</td>
<td>70±2</td>
<td>20±2*</td>
<td>43±3*</td>
<td>13±2†</td>
<td>189±7</td>
</tr>
</tbody>
</table>

Values are mean±SEM. Hemodynamic measurements in the 4 rabbit groups are shown. MAP indicates mean arterial blood pressure; PP, pulse pressure (systolic–diastolic). Gradient MAP is mean blood pressure drop across coarctation. Combined coarctation is the combination of all 3 coarcted rabbit groups.

*P<0.01 (ANOVA) but no difference among the 3 coarcted groups; †P<0.05 (ANOVA) but no difference in the distal MAP or in the heart rate.

### Table 2. Aortic Dimensions and Degree of Stenosis

<table>
<thead>
<tr>
<th>Coarctation</th>
<th>Wrap Level, mm²</th>
<th>Distal Aorta, mm²</th>
<th>Stenosis, %</th>
<th>Coarcted Area, mm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>No wrap</td>
<td>27±3</td>
<td>28±3</td>
<td>82±3</td>
<td>5±1</td>
</tr>
<tr>
<td>Loose wrap</td>
<td>22±2</td>
<td>31±4</td>
<td>80±2</td>
<td>4±0</td>
</tr>
<tr>
<td>Firm wrap</td>
<td>21±1</td>
<td>26±4</td>
<td>83±1</td>
<td>4±0</td>
</tr>
<tr>
<td>Control</td>
<td>25±2</td>
<td>20±2</td>
<td>0±12*</td>
<td>24±3*</td>
</tr>
</tbody>
</table>

Values are mean±SEM. Aortic areas at wrap level and distal aorta are shown. Wrap level was 2 cm proximal to the coarctation. Distal aorta indicates 2 cm distal to coarctation. All measurements are calculated for minimal dimension during cardiac cycle. There was no statistical difference at the wrap level (ANOVA, P=0.24), indicating that external wrap did not statistically constrict the aorta. There was no statistical difference in aortic dimension distal to coarctation but a trend toward poststenotic dilation (ANOVA, P=0.11). Significant stenosis was present in the 3 hypertensive groups, calculated as 100×(1−area of stenosis divided by area of proximal aorta at wrap level).

Coarcted area is area of aorta under cable tie. Significant coarctations were equally created in the coarcted groups.

*P<0.001 but no difference among 3 coarcted rabbit groups.
abdominal aorta of the coarcted animals (12±1%) was reduced compared with that of the noncoarcted control animals (19±1%, P<0.002). In the externally wrapped segment of aorta proximal to the coarctation (level B), aortic wall motion was reduced and was no different from the noncoarcted control value (Table 3). The animals with the loose external wrap had more wall motion (19±2%) than did the animals with the firm wrap (10±3%, P<0.05), but wall motion in both groups was significantly less than that in the nonwrapped coarcted group (28±3%), and wall motion in both groups was no different from that in the noncoarcted control group (15±2%, Table 3).

**Intimal and Medial Area**

Significant atherosclerotic plaque was grossly visible in the proximal aorta of the coarcted animals, whereas none was visible in the proximal aorta of the noncoarcted control animals. Intimal plaque cross-sectional area in the proximal aorta was increased 40-fold in the coarcted groups compared with the noncoarcted control group (Table 4). The segments of proximal aorta in coarcted animals that were externally wrapped did not develop significant intimal plaque, and intimal cross-sectional area was not significantly different from that in noncoarcted control animals (Table 4).

Plaque inhibition occurred in the loosely and firmly wrapped groups (Figure 3).

No atherosclerotic plaque was visible in the aortas distal to the coarctation, and the intimal cross-sectional area was no different in coarcted animals and in noncoarcted control animals (Table 5).

The medial area decreased in a steplike fashion among the 4 sites measured: proximal aorta, wrap level, distal thoracic aorta, and abdominal aorta, reflecting the smaller size of the aorta progressing from proximal to distal. Except for the proximal aorta, no difference in medial area among the 4 rabbit groups was detected. Calculated ratios of intimal to medial area were markedly increased in the unwrapped compared with wrapped segments of the proximal aorta in coarcted animals, reflecting the marked difference in intimal area.

**Discussion**

The findings in the present study include the following: (1) In the hypercholesterolemic rabbit model, intimal plaque, wall motion, mean arterial blood pressure, and pulse pressure are increased proximal to an aortic coarctation. (2) Reduction of aortic wall motion reduces plaque formation despite hypertension.

The clinical manifestations of hypertension and its association with coronary artery disease1,2 and peripheral occlusive disease3–6 are well known. Experimental studies have also indicated that hypertension enhances atherosclerosis. Surgically created aortic coarctations in hypercholesterolemic primates produce hypertension and promote atherosclerosis in the proximal aorta and coronary and carotid arteries.10,11 Similar studies using hypercholesterolemic rabbits have also shown increased aortic atherosclerosis proximal to an aortic coarctation.9,12 Our finding of increased plaque proximal to the coarctation is in agreement with previous investigations. The mechanism by which hypertension potentiates atherosclerosis is unknown. Some investigators have suggested that hypertension induces alterations in sodium and calcium influx, wall composition, and vasoactive hormones and increases monocyte and leukocyte adhesion.15,16

Hypertension is typically thought of as elevated mean arterial pressure, but studies have demonstrated that pulse pressure and alterations in diastolic blood pressure (in-

### Table 3. Wall Motion

<table>
<thead>
<tr>
<th>Coarctation</th>
<th>Proximal Aorta, %</th>
<th>Wrap Level, %</th>
<th>Distal Aorta, %</th>
<th>Abdominal Aorta, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No wrap</td>
<td>26±1</td>
<td>28±2†</td>
<td>13±4</td>
<td>12±2</td>
</tr>
<tr>
<td>Loose wrap</td>
<td>33±5</td>
<td>19±2‡</td>
<td>21±3</td>
<td>13±2</td>
</tr>
<tr>
<td>Firm wrap</td>
<td>29±3</td>
<td>10±3</td>
<td>15±2</td>
<td>10±3§</td>
</tr>
<tr>
<td>Control</td>
<td>17±2*</td>
<td>15±2</td>
<td>16±2</td>
<td>19±1</td>
</tr>
</tbody>
</table>

Values are mean±SEM. Wall motion is calculated as (maximum luminal area−minimum luminal area)/minimum aortic luminal area×100; it is the cyclic variation in luminal area from diastole to systole. Proximal aorta indicates 4 cm proximal to coarctation; wrap level, 2 cm proximal to coarctation; and distal aorta, 2 cm distal to the coarctation. Wall motion is increased proximal to a coartration but is reduced by the external wrap.

• P<0.001, no difference among 3 coarctation rabbit groups; † P<0.001, no wrap greater than control and both wrap groups (no difference between wrap groups and control); loose wrap wall motion greater than firm wrap), and § P=0.05, firm wrap less than control.

### Table 4. Morphometry: Proximal Thoracic Aorta

<table>
<thead>
<tr>
<th>Coarctation</th>
<th>Proximal Intima, mm²/100</th>
<th>Proximal Media, mm²/100</th>
<th>Proximal Intima/Media Ratio</th>
<th>Wrap Intima, mm²/100</th>
<th>Wrap Media, mm²/100</th>
<th>Wrap Intima/Media Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No wrap</td>
<td>39±9</td>
<td>4.8±0.4†</td>
<td>9.2±3</td>
<td>30±3‡</td>
<td>3.6±0.5</td>
<td>9.1±1.4‡</td>
</tr>
<tr>
<td>Loose wrap</td>
<td>51±12</td>
<td>4.0±0.2</td>
<td>12.6±3</td>
<td>6±2</td>
<td>3.3±0.4</td>
<td>2.0±0.7</td>
</tr>
<tr>
<td>Firm wrap</td>
<td>34±5</td>
<td>3.5±0.2</td>
<td>10.0±2</td>
<td>4±2</td>
<td>2.8±0.2</td>
<td>1.3±0.5</td>
</tr>
<tr>
<td>Control</td>
<td>0.7±0.4*</td>
<td>3.7±0.1</td>
<td>0.2±0.1*</td>
<td>1±1</td>
<td>3.1±0.3</td>
<td>0.3±0.5</td>
</tr>
</tbody>
</table>

Values are mean±SEM. Intima and media areas were calculated from aortic tissue specimens by using quantitative morphometry. Units of area are square millimeters×0.01. Intima/media ratio is intima to media ratio×100. Proximal denotes 4 cm proximal to coarctation; wrap indicates the wrap level. Atherosclerosis was significantly increased proximal to aortic coarctation but was reduced by the wrap.

• P<0.001, no difference among the 3 coarcted groups; † P<0.001 for no wrap vs other 3 groups; ‡ P<0.01 for no wrap vs other 3 groups.
creased and decreased) may be a risk factor for atherosclerosis. Sutton-Tyrrell showed that increased pulse pressure was correlated with increased carotid stenosis. The difficulties with most of these studies is that it is not known whether increased pulse pressure causes atherosclerosis or whether atherosclerosis modifies the compliance characteristics of arteries, thus increasing the pulse pressure. Wall motion is a function of pulse pressure but is also dependent on pulsatile waveform, external tissue support, and properties of the vessel wall. The most likely explanation for the enhanced wall motion proximal to the coarctation is that the pulse pressure was increased.

Lyon et al previously measured aortic wall motion proximal and distal to an aortic coarctation. They found that aortic wall motion and plaque area were reduced distal to the coarctation. This suggested that reduction in aortic wall motion distal to the coarctation may be responsible for plaque inhibition, whereas there was no increase in wall motion or plaque formation proximal to the aortic coarctation. Thubrikar et al placed acrylic liquid over the aortic bifurcation and renal ostia of anesthetically induced hypotensive rabbits and demonstrated reduced intimal thickening in chronically normotensive hypercholesterolemic rabbits. The authors suggested that reduced wall stress and not reduced wall motion accounted for the findings. Although wall motion was not measured in their study, wall motion was probably reduced. Wall stress cannot be directly measured but will vary over the cardiac cycle. Wall motion and stress are to some extent interrelated, and reduction in wall motion probably indicates reduction in cyclic wall stress. External wrapping of vein grafts has been studied in detail, but the reduction in the normal wall proliferative response to an arterialized vein due to the external wrap cannot be correlated with the study of arteries and atherogenesis in the presence of hypertension. In addition, wall motion was not measured in these studies.

Wall motion was increased proximal to the coarctation but was decreased by the loose wrap and further decreased by the firm wrap. The mean arterial blood pressure was equally elevated (25 mm Hg) in all 3 hypertensive rabbit groups compared with the control rabbit group, and the systolic blood pressure was quite elevated (41 mm Hg) in the 3 coarctation groups (115 mm Hg) versus the control group (74 mm Hg). Even in the presence of this significant hypertension, intimal thickening was significantly reduced with the external wrap. The degree of stenosis was the same in the 3 coarctation groups. In addition, the heart rates, cholesterol levels, and weights were similar among all the groups. Further evidence to indicate that the reduction in wall motion is the explanation for the reduction in atherosclerosis can be elicited by examining the

### Table 5. Morphometry: Distal Thoracic Aorta and Abdominal Aorta

<table>
<thead>
<tr>
<th>Coarctation</th>
<th>Distal Intima, mm²/100</th>
<th>Distal Media, mm²/100</th>
<th>Distal Intima/Media Ratio</th>
<th>AA Intima, mm²/100</th>
<th>AA Media, mm²/100</th>
<th>AA Intima/Media Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No wrap</td>
<td>0 ± 0</td>
<td>2.7 ± 0.4</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>1.4 ± 0.2</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Loose wrap</td>
<td>0.1 ± 0.1</td>
<td>2.2 ± 0.2</td>
<td>0.1 ± 0.1</td>
<td>0 ± 0</td>
<td>1.1 ± 0.1</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Firm wrap</td>
<td>0.3 ± 0.3</td>
<td>2.5 ± 0.2</td>
<td>0.1 ± 0.1</td>
<td>0 ± 0</td>
<td>1.0 ± 0.1</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Control</td>
<td>0.1 ± 0.1</td>
<td>2.7 ± 0.1</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>1.4 ± 0.2</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>

Values are mean ± SEM. Intima and media areas were calculated from aortic tissue specimens by using quantitative morphometry. Units of area are square millimeters × 0.01. Intima/media ratio is intima to media ratio × 100. Distal indicates 2 cm distal to coarctation; AA, abdominal aorta at the level of the renal arteries. Minimal to no plaque was present distal to the coarctation.
proximal aorta. At this level, wall motion was quite elevated, and plaque was consistently elevated in all 3 coarctation groups. At the wrap level, no difference in intima area was detected between the loosely wrapped and firmly wrapped groups, even though wall motion was further reduced by the firm wrap. The degree of intimal thickening was minimal in the loosely wrapped group, and to detect a difference at this early time point would have been very difficult. Another explanation for this finding may be that the 31% reduction in wall motion between the coarcted group with no wrap and the coarcted group with loose wrap may have been sufficient to inhibit the majority of atherosclerosis attributed to hypertension. In addition, the wall motion in the loosely wrapped group had returned to control levels. The loose wrap reduced wall motion probably as a result of the formation of surgical scarring. The present study was unable to discern the relative importance of mean arterial blood pressure versus wall motion (or pulse pressure), but clearly, wall motion is an important component. The stretch of the vessel wall may allow the passage of atherogenic molecules.

Low wall shear stress has received much attention in the literature with respect to atherosclerosis. These changes in intimal thickening cannot be explained by alterations in flow, shear, or oscillatory shear. Although flow was not measured, the 3 coarcted rabbit groups were identical, hemodynamically and anatomically, by all measured variables. The only effect shear may have is if there is a reduction in the luminal diameter of the aorta induced by the wrap (by increasing flow velocity). As Table 2 indicates, no statistical difference in diastolic luminal area was detected (ANOVA, P = 0.231). One half of the rabbits randomly underwent angiography. An ~10% reduction in area was noted in the subset of rabbits with firm wrap. However, all 3 rabbits in the coarcted group with loose wrap that underwent angiography had no evidence of stenosis at the wrap level. These findings strongly suggest that shear is not a significant factor in this model. Glass model dye visualization studies of an aortic coarctation demonstrate little change in shear proximal to a stenosis.

The mechanism by which reduced wall motion inhibits cellular proliferation and reduced intimal thickness is not known. It may be that reduced cyclic stretch of the vessel wall during the cardiac cycle inhibits the uptake of cholesterol, lipoproteins, and other molecules and that endothelial cell adhesion may be reduced. External wrapping of any vessel reduces wall stress, which may alter endothelial cell structure and function or induce endothelial cell enzymes or autocrine factors. An inflammatory reaction between the adventitia and external wrap is probably formed, and it may also be responsible for reduced intimal proliferation. The inflammation may reduce the vasorum or inhibit heparin-binding growth factors.

Intravascular ultrasound was used because of its ability to display the change in aortic luminal dimensions during the cardiac cycle. Intravascular ultrasound is currently being used to study plaque in the coronary arteries. In a previous study of wall motion in our laboratory, ultrasound crystals were placed on the outside of the aorta. The use of intravascular ultrasound permitted measurement of the area by tracing the luminal contours and also permitted the measurement of wall motion at many locations with relative ease.

In summary, this experimental model of aortic coarctation induces rapid intimal plaque deposition in the aorta proximal to the coarctation, with sparing of the aorta distal to the coarctation. The hypertensive proximal aorta experiences not only increased mean arterial blood pressure but also increased pulse pressure and cyclic wall motion. This hemodynamic environment results in rapid cellular proliferation and lipid uptake in hypercholesterolemic animals but not in normocholesterolemic animals. In the present study, we have shown that wall motion can be inhibited by an external rigid support placed either loosely or firmly. This reduction in wall motion inhibited plaque deposition despite increased blood pressure, increased pulse pressure, and marked hypercholesterolemia. Thus, wall motion appears to be a critical factor necessary for cellular proliferation, lipid uptake, and intimal plaque formation.

References


