Contribution of Dynamic Vascular Wall Thickening to Luminal Narrowing During Coronary Arterial Constriction

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SUMMARY  Available estimates of the ratio of wall thickness to luminal radius of human coronary arteries and certain geometrical assumptions were used to calculate the amounts of vascular smooth muscle shortening required to produce specific changes in luminal diameter for hypothetical "normal" and stenotic arteries. The results indicate that even modest mural thickening due to disease may act as a "lever" in translating physiologic degrees of medial smooth muscle shortening into critical luminal obstructions, providing the diseased segment maintains some pliability. The possibility of acute luminal occlusion occurring at stenotic sites as the result of "normal" vasomotion is illustrated. The appropriate use of the term coronary arterial "spasm" is discussed in light of these observations.

THE ANGIOGRAPHER’S VIEW of the coronary arteries is obtained from “shadows” cast by the blood-contrast medium as it is confined by the vessels’ luminal borders. Quantitation of vasomotion observed by angiography is thus limited to comparing the luminal diameters in two or more states of vasomotion. Because we cannot see the arterial wall itself, we do not always appreciate the changes occurring in it that produce the variations of luminal dimension we call "vasomotion."

In this paper, I use elementary geometric principles to reconstruct some of the changes that can occur in the wall of a large coronary artery during vasomotion. Understanding of these changes is essential before a rational definition of coronary arterial "spasm" can be made.

The Arterial Wall

The wall of a large coronary artery is shown in transverse cross section in figure 1. It consists of three main layers. The inner coat (tunica intima) is bounded internally by vascular endothelium, which lines the lumen, and externally by the internal elastic membrane. In the adult coronary artery there is a subendothelial layer of fine areolar tissue and just internal to this a musculoelastic lamina, consisting of irregularly arranged elastic fibers interspersed with smooth muscle cells. The intima of the large coronary arteries tends to be thicker than the intima of comparably sized muscular arteries elsewhere in the body, and during middle age the intimal thickness is several times that of the media.1 2

The middle coat (tunica media) consists mainly of spirally oriented smooth muscle cells, the contraction and relaxation of which result in active vasomotion of the vessel.
The outer coat (tunica adventitia) consists of loosely arranged collagen, with some elastic tissue that coalesces near the inner border to form an external elastic membrane. The outer margins of the adventitia blend indistinctly into the surrounding tissues and hence its width is really indeterminate. With this limitation, the ratio of total wall thickness (h) (including adventitia) to luminal radius (R) of most large and medium-sized arteries distended at physiologic pressures has been estimated at 0.10–0.20. Taking into account the increased thickness of the coronary arterial intima and excluding the adventitia, the ratio h:R in the adult large coronary artery at physiologic distending pressures will probably be 0.1–0.3 in persons younger than 40 years old, although in older persons it may exceed this range owing to progressive intimal thickening.  

**Geometric Considerations**  
Let us assume a normal coronary artery that is circular in cross section when distended by a normal blood pressure and has an outer radius Rₒ (including the media but excluding the adventitia) and inner (luminal) radius Rᵢ. Assume that the wall thickness (h) is uniform around the circumference and that h = Rₒ - Rᵢ = 0.2Rᵢ. Figure 2A is a diagram of such an artery. For practical purposes, the material of the normal arterial wall is plastic but incompressible. If we assume that there is no change in the length of the artery as the result of changes in its diameter, and no extrusion of tissue from the constricted area into non-constricted, adjacent parts of the artery, then at any point of the artery the area Aᵦ of the arterial wall on a transverse cross section of the vessel will be constant regardless of the state of its contraction or dilation: Aᵦ = π (Rₒ² - Rᵢ²) = a constant.

As vasoconstriction occurs, the luminal radius decreases proportionately more than the outer radius of the vessel and the wall thickness increases (fig. 2A). At coronary arteriography in normal, conscious human subjects, there is evidence of a significant "tone" of the vascular smooth muscle maintaining the arterial size. Vasodilators such as nitroglycerin cause
as much as 20–30% increase in luminal diameter, while vasoconstrictors such as ergonovine maleate or epinephrine cause as much as 20%–30% decrease in diameter. Spontaneous decreases in luminal diameter of 20% have been seen during the course of coronary arteriography in normal humans. These data suggest that major coronary arteries can, under physiologic conditions, approximately double their luminal diameter from their most constricted to their most dilated state.

The degree of luminal narrowing produced by a given shortening of outer layers of medial smooth muscle is critically dependent on the wall thickness contained within those smooth muscle layers. In figure 3 the percent decreases in luminal radii expected from specific decreases in outer arterial circumferences are plotted for different h:R ratios. Significant narrowing of normal vessels can be produced within the physiologic ability of vascular smooth muscle to contract (30% shortening) when h:R ratios of the dilated artery exceed 0.2. Moreover, as the luminal narrowing produced by vasoconstriction exceeds about 70%, only relatively minute further shortening of the smooth muscle is needed to occlude the vessel completely, even with low h:R ratios. The increased wall thickness acts as a lever to magnify the effects of smooth muscular contraction on luminal diameter.

These magnifying effects of wall thickness may be greatly exaggerated in the diseased coronary artery, where the highest h:R ratios are seen because of subintimal atheromatous deposits. Despite the pathologic studies of Leary a half century ago, it has been until recently a common supposition that significant atherosclerosis caused an arterial segment to become rigid, preventing vasomotion at that point. In reality the atherosclerotic involvement of the arterial wall is frequently eccentric, leaving normal wall over part of the circumference. Moreover, even high-grade, apparently concentric stenoses can change their diameter under the influence of drugs that affect arterial smooth muscle. In figure 4 the decrease in luminal diameter of a normal segment of coronary artery that an angiographer might observe as the result of a provocative test or from spontaneous vasoconstriction is plotted against the decrease in luminal diameter of an adjacent stenotic segment expected to result from the same amount of outer wall circumferential shortening that caused the decrease in luminal diameter of the normal arterial segment. Even with stenoses of only 20–30%, significant decreases in diameter of stenotic segments, even complete obstruction, could be seen with decreases in the normal adjacent lumen in the range that has actually been observed in coronary arteries of normal persons. With stenoses of about
FIGURE 4. The percent decrease in luminal diameter in a normal segment of artery adjacent to a stenosis is plotted on the ordinate and the percent decrease in diameter at the stenosis expected to result from the same degree of outer wall circumferential shortening that caused the observed decrease in lumen in the adjacent normal segment of vessel is plotted on the abscissa for hypothetical stenotic coronary arteries. Curves are plotted for stenoses of 10%, 20%, 40%, 60% and 80% in the dilated artery. These curves make no assumptions about h:R, ratios of the normal vessel wall and are valid for all such h:R, ratios. To estimate the outer wall circumferential shortening required to produce such luminal changes, select the appropriate h:R value and refer to figure 3.

80% and greater, the amount of decrease in luminal diameter of the adjacent normal segment that would represent production of a complete occlusion at the stenosis is less than the resolving power of coronary cineangiography. For a 90% stenosis, 0.5% decrease in normal lumen diameter would represent a complete occlusion at the stenotic site. This graph assumes complete translation of increased circumferential smooth muscle tension at the stenosis into shortening of that muscle equivalent to what is occurring in the normal segment of artery. In reality, this does not occur because the artery is more rigid at the stenotic point, and the decrease in diameter at the stenosis would be expected to be less than that predicted from figure 4.

The magnifying effect of a stenosis on changes in lumen size during vasoconstriction is also shown in figure 2. The utility of this view of vasoconstriction can be illustrated by examining data in table 1 from coronary arteriograms before and during episodes of variant angina. The data from Brown et al. were obtained with sophisticated quantitative angiographic techniques, whereas my own observations are based on simpler (but less accurate) methods available to the average angiographer.

In the first case shown in table 1, the spontaneous occurrence of angina with ST-segment elevation in inferior leads (dominant left circumflex circulation) was associated with a diffuse 18–19% decrease in diameter of all major left coronary artery branches and complete occlusion of the circumflex branch at the site of a previous 69% stenosis. Figure 4 shows that an 18% decrease in diameter of the lumen of the normal vessel will, if fully translated to the stenotic point, be more than enough to occlude the vessel. Here, a degree of vasomotion of the left coronary arterial tree that has often been seen spontaneously in normal humans at arteriography is associated with complete occlusion of a coronary artery at a stenotic point. This probably should not be called "spasm."

In the second case in table 1 with a spontaneous attack of angina, there was a 32% decrease in vessel diameter in the normal segments and a 53% decrease in diameter in the stenotic area. Figure 4 shows that a 32% decrease in lumen in the normal segment is more than enough to account for complete occlusion of the vessel at the stenotic point. Hence the vessel wall actually constricted less at the site of the lesion than at the "normal" areas, which is consistent with decreased piability of atherosclerotic plaques. The apparently greater relative change in lumen size at the stenotic site was due to the magnifying effect of shortening of the stenotic vessel wall during vasoconstriction rather than to a hypersensitivity of the smooth muscle at the site of the lesion. Whether this represents coronary "spasm" depends on the normality of a spontaneous 32% decrease in luminal diameter of the "normal" part of the vessel. For a vessel with an h:R ratio of 0.2, this would represent a 21% shortening of the outer circumferential smooth muscle (fig. 3), which is in the range of physiologic possibility.

In the third case, variant angina was pharmacologically provoked and there was clearly a hypersensitivity of the right coronary artery at the site of the mild stenosis, because the normal segment of vessel above the stenosis actually increased slightly in diameter when the stenotic segment narrowed to a nearly complete occlusion. This probably should be called coronary arterial spasm.

Discussion

The above considerations are hampered by the indefiniteness of available anatomic data. Actual measurements of h:R ratios for large human coronary arteries, made with the vessel distended with physiologic pressures, are rare. Thickness of the wall will vary greatly due to age, race, and disease state. The thickness of the coronary smooth muscle layer can be increased by extracardiac disease and decreased by underlying subintimal atherosclerosis. The eccentricities of atherosclerotic and relative stiffness of atheromata can make the geometry of vasomotion different at some diseased sites from that presented here. Clearly, additional studies of h:R ratios of human coronary arteries at physiologic distending pressure are needed, as are
studies of the physical properties of coronary arterial walls at the sites of atherosclerosis.

Undoubtedly, many atheromatous stenoses are rigid enough to be unyielding to the effects of contraction of any smooth muscle left in the wall at that site; these, if circumferential, are truly "fixed" stenoses. But it is just as certain that hemodynamically significant active vasomotion does occur at stenotic regions in some patients.8, 10, 12, 16, 17

Significant coronary obstruction, even complete occlusion, can be dynamically produced by physiologic degrees of vasoconstriction when superimposed on what some have considered insignificant grades of atheromatous stenosis (20–30%). My own angiographic observations of spontaneous or drug-induced dynamic coronary occlusion that caused attacks of variant angina in six patients suggest that the obstruction occurred at the site of a well-defined, often mild-to-moderate, organic stenosis in five of the six cases. This is in agreement with the experiences of others.12, 24 27 In such cases, if the degree of neighboring normal wall motion is within the range normally expected for the circumstances,10, 28 the term coronary arterial "spasm" may not be appropriate. It is semantically useful to extend to larger arteries the concept proposed by Folkow et al.29 and Conway30 for arterioles in hypertension, where the vessels for structural reasons may exhibit an enhanced vascular reactivity, while smooth muscle reactivity remains normal.

That the clinical manifestations of variant angina might be due to normal coronary arterial vasomotion superimposed on an organically narrowed vessel was proposed in the original description of that syndrome by Prinzmetal and co-workers, who carefully avoided the use of the term "spasm."31 Pickering also believed that the use of the term "spasm" should be reserved to indicate a degree of contraction of blood vessels that is clearly abnormal.32

None of these considerations exclude the possibility that, because of unusual stiffness of the wall at a stenotic point, the observed decrease in lumen at the stenosis was the result of extraordinarily strong contraction of circumferential smooth muscle localized only to that part of the vessel. Such a hypothesis is not necessary to explain the changes in vascular diameter in many cases where vasoconstriction at stenotic points produces severe obstruction.

States of arterial hypercontractility and true coronary spasm do exist, as shown by the many cases of dynamic coronary obstruction and even occlusion documented arteriographically in patients with variant angina and "normal" coronary arteries.27, 28, 33–38 Although in some patients it is highly likely that significant atherosclerotic involvement of the vessel at the site of spasm was either not seen on the arteriogram39 or seen and deemed insignificant by the angiographer, in others there are no demonstrable vascular wall abnormalities on postmortem examination.35 Additional careful pathologic examinations are needed of such "normal" coronary arterial segments (shown during life to be involved in spasm) to rule out the possibility that such "spasm" can be due to normal vasomotion in vessels with unusually thick walls, as might have occurred in a patient recently reported by Rizzon et al.40

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WALL THICKENING WITH CORONARY CONSTRICION/MacAlpin

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