Atherosclerosis and Blood Pressure Variability

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In this issue, Johansson et al[1] find that markers of atherosclerosis and inflammation (which is present in atherosclerotic plaques) are associated with postural hypotension. When we stand, >500 mL of blood descend into the legs, decreasing blood pressure. The baroreflex is the initial mechanism called into play to stabilize blood pressure. Blood pressure changes are sensed by the baroreceptors in the carotids and aortic arch and signaled to the brain stem, which initiates an increase in heart rate in a single heartbeat. Sympathetic nerves then lead to vasoconstriction so that blood pressure returns toward baseline levels in ≈20 seconds after standing. When this system fails, postural hypotension ensues. Postural hypotension is not just a risk for falls, it is also associated with an increased incidence of stroke and myocardial infarction.[2]

Baroreflex control of blood pressure slowly deteriorates with advancing age, diminishing both sympathetic[3] and parasympathetic[4] nervous responses to hypertension and hypotension. Loss of baroreflex function is accelerated in hypertension and atherosclerosis. Consequently, the incidence of postural hypotension and episodic hypertension also increases with age and vascular disease. The baroreflex is impaired in subjects with carotid plaque and coronary atherosclerosis.[5] Diminished heart rate variability is a sign of baroreflex loss and is associated with excess cardiovascular mortality and total mortality[6] and predicts coronary artery disease. After a myocardial infarction, depressed baroreflex sensitivity predicted a 280% increase in cardiac mortality.[7] Johansson et al[1] report that proteins associated with atherosclerosis are also associated with impaired blood pressure control. Why should this be so?

Baroreceptors are located near the carotid bifurcation, a common site of atherosclerotic plaque (Figure). Baroreceptors sense blood pressure by responding to stretch of the arterial wall, sending nerve traffic to brain stem centers that regulate autonomic control of blood pressure. When the blood vessels are too rigid to stretch, baroreceptor function is deficient. Rigid carotid arteries are the strongest physiological correlate of a decreased baroreflex. When baroreceptor input is diminished, the autonomic nervous system buffers blood pressure, poorly leading to both hypertension and hypotension.

Baroreflex measurements are not common in clinical medicine, but indicators of diminished baroreflex function are common. A baroreflex deficit often occurs in patients with vascular rigidity from atherosclerosis, a long history of hypertension, or vascular calcification. Patients with a diminished baroreflex may complain of tiredness and postural lightheadedness after a high carbohydrate meal. The same patients have high blood pressures during stress, cold, and particular times of day. Loss of heart rate variability strongly correlates with baroreflex loss,[7] and conversely, respiratory sinus arrhythmia is mediated by intact baroreflexes. Excess blood pressure variability is the most troublesome hallmark of baroreflex loss,[8] and this is best detected by multiple home blood pressures or 24-hour blood pressure monitoring. Ultrasound examination of the carotids may show intima–media thickening and atherosclerosis. Symptoms of hypotension, excess blood pressure variability, diminished heart rate variability and vascular rigidity are common with baroreceptor deficits.

Two of the most vexing problems in the treatment of high blood pressure are symptomatic postural hypotension and episodes of excessively high blood pressure. Excess blood pressure variability makes the diagnosis of hypertension difficult,[8] but signs of target-organ damage such as cardiac hypertrophy, renal insufficiency, and microalbuminuria usually indicate the need to lower blood pressure. Unfortunately, poor baroreflex control of blood pressure makes patients more susceptible to hypotension.[9] Postural symptoms can be worsened by α-adrenergic antagonists such as prazosin, doxazosin, and labetalol, as well as by higher doses of diuretics. Drugs such as tricyclic antidepressants, tamsulosin, older antipsychotics, and marijuana can also cause postural hypotension, a risk for injurious falls. The association of postural hypotension with stroke, myocardial infarction,[2] and early mortality[8] is attributable, in part, to its association with atherosclerosis, but episodes of low blood pressure might also directly compromise circulation. Patients should be asked to record upright blood pressures when they feel lightheaded. They can then be instructed in ways to deal with lightheadedness such as exposure to cold, fluid intake, and isometric exercise. On the contrary, episodes of hypertension can often be dealt with by removing a source of stress. Clinic blood pressures tend to be unreliable when baroreflexes are diminished; elevated on cold days and in novel environments, low during boredom and relaxation. Treatment goals should be guided by both clinic and home blood pressures and drugs selected to avoid hypotension. Several small studies have found that aerobic exercise improves baroreflex function. Although these studies have been too small to detect direct health benefits from an improved baroreflex, the cardiovascular benefits of exercise are well established.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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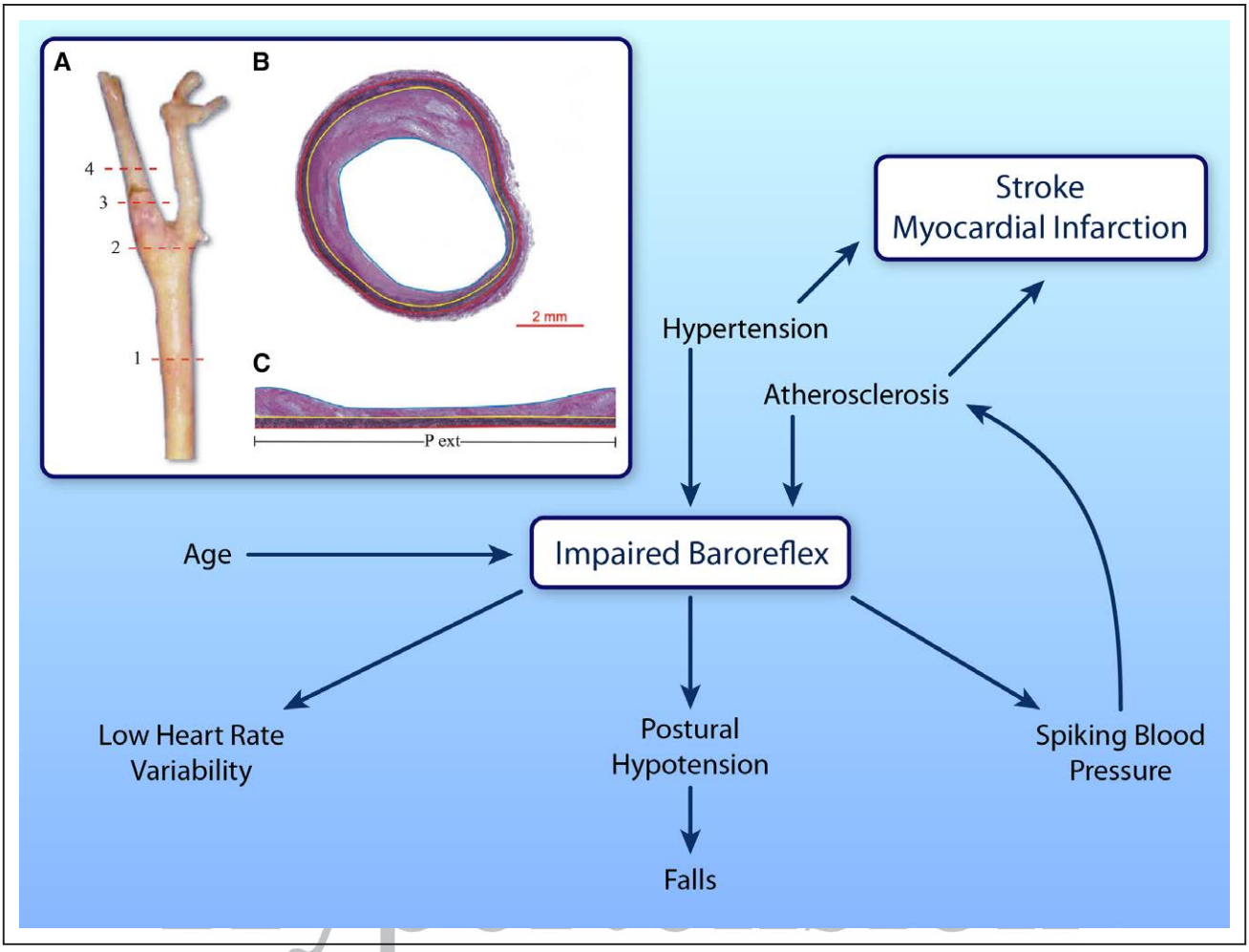

Figure. Atherosclerosis and the baroreflex. The carotid artery at the bifurcation (**A**). The common carotid (1) leads to the carotid sinus that extends from line (2) to line (3) leading to the internal carotid artery (4). The carotid sinus is the site of atherosclerosis shown in cross-section (**B**) and lengthwise (**C**). The external elastic lamina is stained red; the internal lamina stained yellow. Atheromatous plaque internal to the laminae limits stretch of the baroreceptors in the wall of the carotid sinus. When atherosclerosis of the carotids impairs baroreflexes, postural hypotension and episodic blood pressure spikes follow. Histology insert reprinted from Suemoto et al[11] with permission. Copyright © 2009, The Authors.

Even normotensive individuals with diminished baroreflex function have special medical risks and needs. The baroreflex decreases with advancing age[4] and carotid[5] and coronary[10] atherosclerosis. This partly explains the wide blood pressure swings seen in the elderly. When properly taken into account, baroreflex deficits may alter the choice of drugs, diagnosis of hypertension, advice to patients, screening for postural hypotension, and treatment goals for high blood pressure. A common sign of impaired baroreflexes is when patients fail to appropriately raise or lower their heart rate in response to an acute change in blood pressure. In the article by Johansson et al,[1] the subjects with orthostatic hypotension decreased their systolic blood pressure with standing by 46 versus 11 mm Hg in the controls, yet they increased their heart rate only 4 bpm more than the controls. This failure to increase heart rate enough to help maintain blood pressure is characteristic of an inadequate cardiovagal baroreflex response. Atherosclerosis should make us ask about postural symptoms and suspect baroreflex loss. On the other hand, evidence of baroreflex loss should make us suspect vascular disease and the need for treatment to slow progression. Diminished baroreflexes provide a characteristic clinical picture that is often associated with diffuse atherosclerosis.[5–7,10] These patients have increased cardiovascular risk and may be candidates for moderate- to high-dose statins and antiplatelet therapy, as well as careful blood pressure regulation that avoids drugs that cause postural hypotension.

Elderly hypertensives have wider blood pressure swings than young normotensives. This is often attributed to hardening of the arteries. Although this explanation is correct, it is incomplete and of little practical use. A more complete explanation is that hardening of the arteries impairs stretch of the baroreceptors leading to diminished neural input to brain stem autonomic control centers and thereby to diminished autonomic output to the cardiovascular system (Figure). The consequence is a failure to return high or low blood pressure back to baseline. This more complete understanding of why atherosclerotic arteries are associated with postural hypotension and episodic hypertension has practical use. Patients with wide blood pressure swings should not be treated with drugs that further impair autonomic responses. Their blood pressure extremes are sometimes best

treated with behavioral modifications that remove the stimulus to the blood pressure change. When patients experience excess blood pressure variability, a review of their heart rates and blood pressures can determine whether impaired baroreflexes are a likely cause. The presence of impaired baroreflexes should alert to the likelihood of postural hypotension, episodic hypertension, and vascular rigidity from diffuse atherosclerosis.

Disclosures

None.

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