Arterial Baroreflex Modulation of Sympathetic Activity and Arterial Wall Properties

New Evidence

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See related article, pp 98–104

The arterial baroreflex is among key fast-reacting mechanisms maintaining cardiovascular homeostasis, in particular, regulating blood pressure (BP). Baroreflex influences stemming from stretch receptors located mainly in the carotid arteries and in the aortic arch are triggered by changes in transmural pressure of these vessels. The effector arm is directed toward cardiac and vascular targets and provides rapid feedback reactions to changes in BP (because of, eg, postural changes), mainly through reflex modifications of cardiac output (including vagally mediated changes in heart rate) and of arterial tone, through changes in sympathetic activity. This apparently simple model of arterial baroreflex is in real life made much more complex because of central integration of afferent baroreceptor influences with influences from other areas (eg, cardiopulmonary receptors and chemoreceptors), as well as with influences from cortical and subcortical centers.

Arterial baroreflex function can be evaluated in a laboratory environment and in daily life conditions through different techniques. Baroreflex control of heart rate can be investigated by assessing the reflex changes in RR interval in response to changes in systolic BP: (1) induced by intravenous injection of drugs affecting BP with no major direct effect on the heart (eg, phenylephrine or nitroglycerine); (2) triggered by the Valsalva maneuver (a less specific method); and (3) occurring spontaneously, using time domain (sequence technique), or frequency domain (coefficient analysis methods). Assessment of the sympathetically mediated reflex changes in peripheral resistance and BP is more difficult and requires either the estimation of changes in efferent muscle sympathetic nerve activity in response to diastolic BP changes induced by vasoactive drugs and/or the assessment of BP reflex changes induced by direct carotid baroreceptor stimulation or deactivation (neck collar technique). With all of these methods, baroreflex sensitivity (BRS) is defined as the size of effector response (change in heart rate, muscle sympathetic nerve activity, or BP) induced by a unit change in transmural carotid or aortic pressure. When using baroreceptor stimulation/unloading laboratory techniques, this is achievable over a wide range of transmural pressures, allowing a precise definition of the baroreflex stimulus-response curve in different individuals.

The overall baroreflex modulation of cardiovascular parameters has two distinct components. The first one is the relationship between changes in carotid/aortic transmural pressure and the corresponding changes in carotid/aortic diameter. This component depends on arterial wall rigidity and represents one of the principal determinants of the degree of baroreceptor stretching/relaxation in response to a given pressure change (mechanical component). The second one is the link between changes in carotid/aortic diameter and the subsequent changes in cardiac and vascular responses, which depend on the features of afferent inputs to brain stem centers, on the central integration of these inputs, and on the efferent firing to cardiac and vascular targets (neural component).

Studies on baroreflex cardiovascular modulation have emphasized the important pathophysiologic role of arterial baroreflex in different clinical conditions as well as its role as an independent risk predictor in patients with cardiovascular disease. However, only recently the development of non-invasive techniques for the study of arterial properties has made it possible to investigate more in depth the relationship between rigidity of the arterial wall and baroreflex function. In fact, given that baroreceptors respond to the extent of stretching/relaxation of carotid/aortic arterial walls rather than to BP, per se, one may expect that, in subjects with stiff arteries, which distend less than more elastic vessels in response to BP changes, baroreflex responsiveness will be reduced. This reasonable pathophysiological hypothesis was supported by studies showing that, in humans, increased local carotid stiffness may be associated with reduced cardiovagal BRS. Conversely, very limited information is available on the possible relation between arterial stiffness and the effectiveness of baroreflex modulation of the arterial tone.

The article by Okada et al, published in the current issue of Hypertension, was aimed at offering novel information in this regard. In 61 elderly subjects (30 men and 31 women), local arterial stiffness was assessed at carotid artery (ultrasonography) and aortic arch (magnetic resonance) level. Sympathetic BRS was assessed by measuring changes in muscle sympathetic nerve activity in response to diastolic BP changes in resting condition and during the Valsalva maneuver, whereas cardiovagal BRS was assessed by relating RR
interval and SBP beat-by-beat values during the Valsalva maneuver. The results clearly demonstrate a significant inverse correlation between the degree of carotid stiffness (\(\beta\)-stiffness) and sympathetic BRS, whereas the data in relation to aortic stiffness are less clear (see below).\(^8\)

The main conclusion of the study that vascular BRS relates to arterial wall elasticity represents new information and nicely complements the findings reported previously on the relation between arterial stiffness and cardiac BRS.\(^6,7\) The study by Okada et al,\(^8\) however, offers intriguing information also with regard to gender differences in the relation between arterial stiffness and sympathetic BRS. Sympathetic BRS was overall lower in elderly women than in men, and, whereas the relationship between sympathetic BRS and arterial stiffness had the same slope in both genders, it was shifted upward in women (ie, at the same level of arterial stiffness, the baroreflex response was always smaller in women). Given the relatively small study sample size, however, one cannot exclude that this shift represents a statistical error, and, thus, this interesting result should be confirmed in a larger population. An additional interesting finding is that, in women, cardiac baroreflex response was also less pronounced than in men but only when considering systolic BP increases (phase IV of Valsalva maneuver) and not systolic BP decreases (phase II). Although the phenomenon of baroreflex hysteresis (ie, different sensitivity with different direction of BP change) is well known,\(^9\) the fact that it may differ between genders is less well documented.\(^10\)–\(^12\) This finding, however, given the limited specificity of the Valsalva maneuver in assessing arterial baroreflex sensitivity,\(^2\) should also be confirmed using a more appropriate methodology.\(^13\)

Okada et al\(^8\) suggest that gender differences in BRS may contribute to determination of BP levels and, thus, be relevant in the pathogenesis of hypertension.\(^8\) However, impaired baroreflex function does not majorly affect differences in average BP but plays a crucial role in determining increased BP variability.\(^14\)–\(^15\) In fact, an interesting practical implication of the findings by Okada et al\(^8\) is that increased arterial stiffness, both directly and through the impairment of baroreflex modulation, might favor an increase in BP variability, which might, in turn, further contribute to organ damage\(^16\)–\(^17\) and to higher risk of cardiovascular events.\(^18\) It might also lead to the increased speed of BP changes that characterize beat-by-beat BP fluctuations in hypertensive patients.\(^19\)

A final relevant methodologic indication provided by the study by Okada et al\(^8\) is related to the finding that, when aortic BP was derived from radial artery waveform by transfer function was used to compute aortic stiffness, no relationship with sympathetic BRS was found; conversely, when central BP was derived from carotid artery waveform, a significant relationship was evident. This supports the view that the accuracy of central BP estimation with transfer function of radial waveform should not be taken for granted.\(^20\)

The main limitation of the study by Okada et al,\(^8\) duly acknowledged by the authors, lies in the fact that the information obtained in elderly normotensive subjects may not be readily extrapolated to populations with different characteristics in terms of arterial properties (eg, younger subjects) or autonomic function (eg, obese or diabetic subjects), and further studies in such populations are needed. Another possible limitation is the use of indirect techniques, which, while being noninvasive and simple, are also more susceptible to random and systematic errors. This is the case when using the Valsalva maneuver because of its limited specificity in assessing BRS and also when peripheral BP values (brachial or finger BP) are used to estimate carotid/aortic BP, that is, to assess the stimulus directly inducing carotid/aortic distension and, thus, baroreflex response.

In summary, the study by Okada et al\(^8\) provides new and valuable information on the link between arterial wall properties and reflex sympathetic cardiovascular control. It also indicates the presence of important gender differences in this regard. Its results open interesting research perspectives in the field of aging physiology and pathophysiology. They may also be relevant to a better understanding of the link between arterial stiffness and BP variability, the possible contribution of which to increased cardiovascular risk has recently been matter of lively discussion.

Disclosures

None.

References


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