The Common Carotid Circulation in Patients With Essential Hypertension

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We review carotid artery hemodynamics in hypertensive men, with particular reference to common carotid artery diameter and blood flow, and emphasize the changes in artery diameter and compliance implied by antihypertensive therapy. (Stroke 1988; 19:1198–1202)

Based on the interpretation of several experimental investigations, the study of carotid hemodynamics in hypertension has long been restricted to the pathophysiologic problems related to high-pressure baroreceptors. Indeed, the arterial wall of the carotid bifurcation contains receptors that play a large part in the regulation of blood pressure and that are considered to be reset to higher pressures in various animal models of hypertension. However, clinical studies indicate that the carotid circulation is involved not only in the pathophysiologic mechanisms of high blood pressure but also in the cardiovascular morbidity and mortality of hypertensive patients. It is widely accepted that the common carotid circulation contributes the major share of cerebral blood flow, the autoregulation of which is an important factor in cardiovascular risk. On the other hand, the initial portion of the internal carotid artery is a selective site of atherosclerotic lesions and therefore plays a particular role in the incidence of cerebral ischemic attacks.

The recent development of Doppler ultrasonographic methods has permitted improved evaluation of the carotid circulation in hypertensive humans. It is possible not only to detect significant stenosis of the internal carotid artery using continuous Doppler systems but also to quantitatively evaluate carotid hemodynamics using pulsed Doppler methods. Data have been obtained in both patients with uncomplicated hypertension and in subjects with stenosis of the internal carotid artery with or without elevated blood pressure. The diameter, blood flow velocity, and blood flow of the common carotid artery have been evaluated. The reproducibility and sensitivity of the method have been shown to be satisfactory when studied both acutely and over the long term.

In this review, our study of human carotid hemodynamics is restricted to hypertensive men, with particular reference to the investigation of common carotid artery diameter and blood flow. The implications of changes in artery diameter and compliance with respect to antihypertensive therapy are particularly emphasized.

Diameter of Common Carotid Artery in Essential Hypertension

The common carotid circulation of hypertensive humans has been studied in ambulant male patients with mild to moderate essential hypertension and compared with that of age- and sex-matched healthy controls. Continuous Doppler examination was performed to exclude significant stenosis of extracranial cervical arteries in both patients and controls. In subjects younger than 45 years, mean common carotid artery diameter was 0.639 ± 0.014 cm in hypertensive patients and 0.651 ± 0.015 cm in normotensive controls. In subjects older than 45 years, mean artery diameter was also similar in patients and controls (0.665 ± 0.018 and 0.653 ± 0.011 cm, respectively). Thus, the carotid artery diameter seemed to be little influenced by age, by blood pressure, or by a combination of both. Brachial artery diameter was simultaneously determined; in hypertensive patients it increased significantly with blood pressure. Finally, it was clearly shown that for a given elevation of mean arterial blood pressure, the response of the vessel is different in the common carotid and brachial arteries of hypertensive patients and depends on the histologic composition of the arterial wall. In particular, the normal common carotid artery diameter in hypertensive patients indicates a shift of the pressure–diameter curve toward higher blood pressures and therefore points to intrinsic modifications of the carotid artery wall in hypertension.

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Whether the shift of the pressure–diameter curve is associated with a change in the slope of the curve, that is, a change in arterial compliance and distensibility, is still a subject of debate. The increase in the carotid-femoral pulse wave velocity observed in hypertensive patients indirectly suggests a reduction in the distensibility of the common carotid artery.13,14 Recently, Van Merode et al11 evaluated the relative changes in common carotid artery diameter during the cardiac cycle using a high-resolution, multigated pulsed Doppler system. The distensibility coefficient was reduced in hypertensive patients, even in young men with borderline blood pressure elevation. Thus, it seems logical to suppose that the unchanged carotid artery diameter of hypertensive patients is associated with a decrease in arterial compliance and distensibility.

The nature of the changes in the viscoelastic properties of the arterial wall in hypertensive patients remains difficult to evaluate. A change in vasomotor tone, an increase in the thickness of the arterial wall, or a combination of both factors have been proposed.15-17 Structural modifications of the arterial wall are expected from simple application of Laplace’s law to the carotid artery system.13,16,17 Histologic studies of carotid arteries from humans with hypertension have shown an increased incidence of tetraploid cells and an increased DNA content, indicating an increased mass of arterial smooth muscle.18

An important area in the study of carotid hemodynamics is the contribution of the arterial wall to the mediation of baroreceptor afferent nerve activity. The carotid sinus contains within its wall much connective tissue (especially elastin) and very little vascular muscle.15-17 The carotid sinus also exhibits low circumferential stiffness. Baroreceptor nerve activity is unquestionably associated with wall deformation as restricting wall distention with plaster casts abolishes baroreceptor-mediated reflexes.17 In this general view, it has also been suggested that the resetting of baroreceptors to higher pressures observed experimentally during the established phase of hypertension is related to reduced distensibility of the blood vessel containing the receptors.4 Evidence of this mechanism in essential hypertension is scanty. Reduced arterial compliance is a characteristic feature of patients with hypertension14 and has been shown to be strongly correlated with reduced baroreflex heart rate sensitivity.19 Changes in carotid sinus activity and a relation with changes in carotid artery diameter have been reported in patients before and after endarterectomy.20 However, the link between these observations and sustained essential hypertension remains tenuous. Recent evidence for an active effect of the carotid artery on the baroreflex mechanisms of hypertensive humans has been provided by the study of vasodilating antihypertensive agents.

The hemodynamic effect of the dihydralazine-like substance cadralazine has been investigated in the common carotid arteries of patients with sustained essential hypertension.12 Four hours after oral administration of 20 mg cadralazine, blood pressure fell markedly and heart rate increased significantly; the diameter of the common carotid artery did not change significantly. However, the tangential tension, which is the product of mean arterial blood pressure and the radius of the artery and thus reflects deformation of the arterial wall, was slightly reduced. The most important finding was the significant relation observed between the change in tangential tension and the change in heart rate: the greater the decrease in tangential tension and hence in deformation of the arterial wall, the greater the increase in heart rate. Since no direct stimulating effect of hydralazine and its derivatives on isolated hearts has been reported,21 the change in heart rate could be used as an index of sympathetic activation.22 On the other hand, the change in heart rate was related exclusively to the change in tangential tension and not with any of its components (i.e., mean arterial blood pressure and common carotid artery diameter). Thus, the results suggested that cadralazine-induced sympathetic activation was related to changes in the carotid artery wall. A cause-and-effect relation might be suggested, the increase in heart rate resulting from changes in carotid artery geometry. An alternative hypothesis is that a common factor, such as activation of the autonomic nervous system, was responsible for changes in both the carotid artery and heart rate. Whichever interpretation may be true, the results clearly indicate that changes in the carotid artery wall participate actively in stimulation of the baroreflex receptor in hypertensive humans and may even act to potentiate the cardiac response.

Cerebral and Common Carotid Artery Blood Flow in Essential Hypertension

In both normotensive and hypertensive humans, cerebral blood flow (CBF) in the resting state is approximately 50 ml/100 g/min.6 CBF is normally autoregulated, that is, kept constant by an intrinsic mechanism during changes in perfusion pressure. Cerebral autoregulation is classically mediated by caliper changes in the small arteries and arterioles of the brain, which constrict when blood pressure rises and dilate when it falls or when intracranial pressure rises. An upper as well as a lower blood pressure limit of autoregulation exist.6 Hence, when blood pressure rises acutely, autoregulatory vasoconstriction ultimately gives way to pressure-forced vasodilatation, and CBF increases. Conversely, below a certain perfusion pressure, autoregulatory vasodilatation becomes inadequate and CBF decreases. In chronic hypertension, CBF autoregulation adapts to high blood pressure. Thus, in hypertensive humans, baboons, and rats,6 the lower limit of autoregulation is shifted toward high blood pressure. A similar shift in the upper limit of autoregulation has been found in baboons with experimental
renovascular hypertension. In humans, only the lower limit of autoregulation has been evaluated and is a mean blood pressure of approximately 110 mm Hg in hypertensive humans and 75 mm Hg in normotensive humans.6,23

A generally accepted concept is that changes in the caliber of arterioles are the major factors contributing to constant CBF. In the cerebral circulation, recent animal experiments have shown that large arteries also contribute importantly to vascular resistance.24 Direct determination of segmental vascular resistance indicates that, while small cerebral vessels make a major contribution to autoregulation during acute increases in blood pressure between 80 and 100 mm Hg, the role of large cerebral arteries becomes increasingly important to the autoregulatory response at blood pressures of >100 mm Hg, that is, in hypertension.24 In that regard, the finding of normal (and not increased) carotid artery diameter in patients with essential hypertension also suggests a contribution of large arteries to the mechanism of increased vascular resistance in the hypertensive human carotidocerebral circulation. Subsequently, the study of common carotid blood flow (CCBF) in essential hypertension seems particularly relevant.

Using pulsed Doppler systems, CCBF has been evaluated as the product of blood flow velocity and the cross-sectional area of the artery.10–12 Mean ± SEM CCBF remains within the normal range in younger (<45 years) patients with sustained essential hypertension (385 ± 20 vs. 410 ± 23 ml/min in controls10). In contrast, mean ± SEM CCBF is significantly reduced in older patients with hypertension (321 ± 14 vs. 385 ± 15 ml/min in controls, p<0.0019). Since in that study continuous Doppler examination excluded significant stenosis of the cervical circulation, the finding in older hypertensive patients must be discussed on the basis of the traditional measures of CBF, indicating little or no influence of uncomplicated hypertension on cerebral perfusion and quantitative CBF. There are several reasons for the apparent discrepancies between CBF and CCBF in uncomplicated essential hypertension. First, considerable interregional blood flow variations may be observed; recent studies in older patients with hypertension indicated a predominant decrease of blood flow in the frontal and temporal regions, probably due to pathologic changes in the territory served by the middle cerebral artery.25 Second, although CCBF is a major component of CBF, CCBF involves both the external and the internal carotid arteries, and therefore the question is whether carotid bifurcation plaques might reduce external carotid blood flow. Finally, whatever the differences between CBF and CCBF in uncomplicated hypertension, both findings point to the same observation: an increase in the carotidocerebral circulation vascular resistance and hence a reduction in the cross-sectional area of small arteries.

Reduction in CCBF may be an important feature in subjects with stenosis of the internal carotid artery and hypertension. The disease promotes atherosclerosis in the extracranial arteries, in particular at the origin of the internal carotid artery and at the bifurcation of the common carotid artery, with a resulting decrease in blood flow. In that regard, CCBF has been studied in both normotensive and hypertensive patients with significant stenosis of the internal carotid artery.9,26,27; in all patients the stenosis, judged by conventional arteriography, was strictly unilateral.26,27 No associated occlusion was observed in the remaining carotidocerebral circulation. On the uninvolved side, mean artery diameter, blood velocity, and blood flow remained within the normal range and were never increased.26,27 In contrast, the involved side showed a significant reduction in artery diameter, blood velocity, and blood flow just proximal to the stenosis.8,26,27 CCBF on the involved side was studied as a function of the degree of stenosis judged by conventional arteriography.26 With stenoses of 40–80% of the arterial diameter, blood flow was reduced (nearly 250 ml/min) and remained practically constant; with stenoses of ≥80%, blood flow decreased abruptly in the common carotid artery (and so involved both the external and the internal carotid arteries). A strongly negative curvilinear relation resulted from this hemodynamic pattern, as previously observed in experimental studies.13 To evaluate the role of hypertension itself with respect to carotid blood flow of subjects with stenosis of the internal carotid artery, they were divided into two groups: those with normal and those with elevated blood pressure.27 Blood flow was significantly reduced in hypertensive patients compared with normotensive controls. Furthermore, CCBF was studied in normotensive controls and hypertensive patients as a function of the degree of stenosis of the internal carotid artery and was expressed as the ratio between blood flow on the involved and the uninvolved side. In both normotensive controls and hypertensive patients, blood flow and the degree of stenosis were inversely related: the higher the degree of stenosis, the lower the ratio, and therefore the more reduced the blood flow of the involved side. However, at any given degree of stenosis, the ratio was lower in hypertensive patients than in normotensive controls. Thus, clinical studies have shown that significant stenosis of the internal carotid artery is responsible for severe reductions of blood flow in the carotid circulation, with greater reductions in hypertensive patients.

Finally, Doppler methods clearly demonstrate that the reduction in CCBF in older patients with essential hypertension may be related to reduction in the cross-sectional area of small arteries, to significant stenosis of the large internal carotid artery, or to both. Thus, the effects of vasodilating antihypertensive agents should differ according to whether the lesions are arteriolar or arterial.
former case, blood pressure reduction should be associated with pure arteriolar vasodilatation; by contrast, in the latter case (stenosis of the internal carotid artery), arteriolar dilatation alone might drastically reduce blood pressure distal to the stenosis.28 Large-artery dilatation, particularly at the site of the stenosis, is preferable as shown by the hemodynamic results of surgery.29 According to this general view, it is important to evaluate the effects of vasodilating antihypertensive drugs on the carotid circulation of hypertensive patients, taking into account the separate effects on small and large arteries.

To this end, hemodynamic measurements were conducted in healthy controls30-32 and in patients with uncomplicated sustained essential hypertension acutely before and 2–4 h.urs after oral administration of three vasodilating drugs with different mechanisms of action.33 Captopril is a classical converting enzyme inhibitor,34 isosorbide dinitrate is a nitroglycerin-like substance, and nitrendipine is a calcium-blocking agent.35 Doses were chosen so as to reduce blood pressure by 10–15% from baseline in the three age-matched subgroups. With isosorbide dinitrate, there was no change in CCBF; the common carotid artery diameter increased significantly, whereas vascular resistance, as an index of the cross-sectional area of small arteries, did not change significantly.33 In contrast, captopril and nitrendipine increased CCBF significantly. Nitrendipine markedly decreased vascular resistance (by dilatation of small arteries), but no change in the caliber of the common carotid artery occurred. On the other hand, captopril induced dilatation of both small (decreased vascular resistance) and large (increased arterial diameter) arteries. This latter finding was further documented in healthy controls, and dose–response curves were obtained with the converting enzyme inhibitors perindopril and ramipril in double-blind studies versus placebo.31,32

In conclusion, our review shows that the common carotid circulation is modified in people with essential hypertension. Hemodynamic changes involve both small (increased vascular resistance) and large (normal diameter despite elevated blood pressure) arteries. Large vessels are probably actively involved in the modifications of the baroreflex mechanisms observed in hypertension. Evaluation of common carotid artery parameters may be useful in assessing the degree of narrowing in subjects with stenosis of the internal carotid artery. In such subjects, CCBF is affected more in hypertensive patients than in normotensive controls for the same degree of stenosis. Finally, in the carotid circulation, vasodilating drugs may dilate small arteries, large arteries, or both, with possible implications for the choice of antihypertensive drugs with respect to preservation of the carotid circulation. Indeed, such assumptions should be limited to this particular circulation and cannot be applied to the general problem of CBF autoregulation in the hypertensive population.

References


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