Arterial Stiffness and Stroke in Hypertension
Therapeutic Implications for Stroke Prevention

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Abstract

Stroke is the second leading cause of mortality worldwide, and the leading cause of death in China and Japan. Its prevention represents a major goal. Identification of primary stroke risk, particularly through newly individualised risk factors including biomarkers of large artery damage such as arterial stiffening, is necessary for determining the appropriate level of intervention. The purpose of this review is to focus on the pathophysiology of arterial stiffness, its predictive value for stroke and the therapeutic implications of this risk factor for stroke prevention. The predictive value of arterial stiffness for stroke was demonstrated in a longitudinal study that included 1715 patients with essential hypertension and measurements of carotid-femoral pulse wave velocity (PWV) [an indicator of arterial stiffness] at entry. Over a mean follow-up period of 7.9 years, during which 25 fatal strokes occurred, PWV significantly predicted stroke (relative risk = 1.39 [(95% CI 1.08, 1.72); p = 0.02 for each 4 m/sec increase) independently of classical cardiovascular risk factors, including age, cholesterol level, diabetes mellitus, smoking and mean blood pressure. Additional longitudinal studies are needed to confirm the predictive value of aortic stiffness on primary and secondary events, in low- and high-risk populations, in various countries, and using different methodologies of arterial stiffness measurement. Drug treatment could prevent stroke through a reduction in arterial stiffness in parallel with correction of cardiovascular risk factors such as hypertension, dyslipidaemia, diabetes mellitus and smoking, all of which are associated with arterial stiffening. In view of the important local actions of angiotensin II on arterial stiffening, drugs interfering with the renin-angiotensin-aldosterone system should be particularly effective. Promising therapeutic strategies to reduce arterial stiffness include taking advantage of the non-lipid-lowering effects of statins and directly targeting the molecular events leading to arterial stiffening, such as formation of advanced glycation end products.

Stroke is the second leading cause of mortality worldwide, and the leading cause of death in China and Japan. Its prevention represents a major goal. Identification of primary stroke risk, particularly through newly individualised risk factors including biomarkers of large artery damage (notably arterial stiffening), is necessary for determining the appropriate level of intervention. Despite the recognised
advantages of global risk assessment, important limitations of this approach have also been identified. Indeed, it is estimated that only half of cardiovascular disease risk is explained by conventional risk factors. Newly individualised risk factors that signal inflammation and large artery damage, such as intima-media thickening, vulnerable atherosclerotic plaque and (most importantly) arterial stiffening, should also be taken into account.

The purpose of this review is to focus on the pathophysiology of arterial stiffness, its predictive value for stroke and the therapeutic implications of this risk factor for stroke prevention.

1. Pathophysiology of Arterial Stiffness

The stiffness of large arteries, including the aorta, represents the ability of large vessels to dampen the pulsatility of ventricular ejection and transform a pulsatile pressure (and flow) at the ascending aorta into a continuous pressure (and flow) downstream at the site of arterioles. In this way, the energy expenditure required for organ perfusion is reduced. With aging, high blood pressure (BP), dyslipidaemia or diabetes mellitus, the large arteries stiffen and pulse pressure (PP) increases at the site of central and peripheral arteries. PP is systolic BP (SBP) minus diastolic BP (DBP). As arterial stiffness increases, the transmission velocity of both the forward and reflected waves increases. This causes the reflected wave to arrive earlier in the central aorta, augmenting pressure in late systole and therefore increasing PP. This augmentation can be expressed as the aortic augmentation index, which represents a percentage of the incremental pressure of aortic PP caused by the reflected wave. Augmentation index is not equal to arterial stiffness, since it depends also on the amount of wave reflection from the periphery, which is influenced by the geometry of the arterial tree and small artery tone.

An increased arterial stiffness can increase the risk of stroke through several mechanisms. First, arterial stiffness may favour the occurrence of cerebrovascular events through an increase in central PP. A growing body of in vitro studies shows that cyclic stretching exerts a greater influence than static load on phenotype and growth of vascular smooth muscle cells. Thus, the amplitude of PP may influence arterial remodelling both at the site of the extracranial and intracranial arteries, increasing carotid wall thickness and the development of stenosis and plaques. The likelihood of plaque rupture and the prevalence and severity of cerebral white matter lesions. In the study by De Leeuw et al., atherosclerosis, indicated by increased common carotid intima-media thickness and plaques, was related to cerebral white matter lesions.

Secondly, measurement of aortic stiffness, which integrates alterations in the arterial wall, may also reflect parallel lesions present at the site of cerebral vasculature. Aortic stiffening accompanying age and cardiovascular risk factors is caused by various phenomena, including breaks in elastin fibres, accumulation of collagen, fibrosis, inflammation, medial smooth muscle necrosis, calcifications, and diffusion of macromolecules within the arterial wall; all of these have also been described at the site of the cerebral vasculature.

Thirdly, coronary heart disease (CHD) and heart failure, which are associated with high PP and arterial stiffness, are also risk factors for stroke. Indeed, arterial stiffness may promote myocardial ischaemia through an increase in PP. One generally accepted view is that arterial stiffness causes a premature return of reflected waves in late systole. This increases central PP and thus SBP and the load on the ventricle, which in turn results in reduced ejection fraction and increased myocardial oxygen demand. Arterial stiffness is also associated with left ventricular hypertrophy, a known risk factor for coronary events, in normotensive and hypertensive patients. The increase in central PP in response to an increase in arterial stiffness corresponds to an elevation in SBP, which raises left ventricular afterload and myocardial work, and to a decrease in DBP, which reduces coronary perfusion; both produce subendocardial ischaemia.
2. Predictive Value of Brachial Pulse Pressure, an Indirect Estimate of Arterial Stiffness

PP increases with increasing aortic stiffness because the pressure wave, which travels from the heart to the periphery (during each cardiac cycle) at a velocity of about 6 m/sec in young healthy subjects, and at about 10 m/sec in middle-aged hypertensive patients, is reflected at some point and returns to the heart. The stiffer the aorta, the faster the return of the reflected wave. The reflected wave is superimposed on the forward wave in late systole, increasing the amplitude of PP and SBP in both the ascending aorta and, to a lesser extent, the peripheral arteries. [3]

For these reasons, early epidemiological studies concentrated on brachial SBP and PP, which were available for large cohorts of patients, with the primary focus being on their predictive value for CHD. Several of these studies identified SBP as a stronger risk factor for CHD than DBP. [21,22] The predictive value of brachial PP for CHD was also well documented. In a study of the Framingham cohort including 1924 subjects between 50 and 79 years of age at baseline, coronary risk increased with low DBP at any level of SBP >120mm Hg. [22] In a larger population of 19,083 normotensive and hypertensive men followed for 20 years, Benetos et al. [21] confirmed that an increased PP was a strong predictor of myocardial infarction, and that this could be observed in both normotensive and hypertensive subjects, particularly in men aged >55 years. Brachial PP is also a strong independent determinant of recurrent events after myocardial infarction in patients with impaired left ventricular function, [23] of risk of heart failure in the elderly [24] and of all-cause mortality in the general population. [21]

The association between BP and risk of stroke is strong and continuous. [25] Although mean BP (MBP) has been found to be the best predictor for stroke in some studies, [21,26-28] a number of epidemiological studies also identified SBP as a stronger risk factor for stroke than DBP [29-33] suggesting a greater predictive role for PP than MBP. [34] Moreover, as expected in older patients with systolic hypertension and a high degree of arterial stiffness, conventional and ambulatory PP are better predictors of adverse outcomes than conventional and ambulatory MBP. [35]

The relationship between arterial stiffness and PP involves wave reflections, and short stature is associated with a short travel time and increased reflections. [3,36] It is tempting to relate the fact that stroke is the leading cause of mortality in China and Japan to the shorter stature of inhabitants of these countries, since a short stature is associated with increased central PP. [30] However, in a recent epidemiological study in Chinese steelworkers, MBP was a better predictor for stroke than PP. [28]

Several findings suggest that increased arterial stiffness may be predictive of cerebrovascular events through an increased PP locally, at the site of cerebral arteries. Indeed, brachial PP is associated with carotid artery disease, including increased intima-media thickness and plaque area. [9-11] PP is a major determinant of small artery disease, particularly hypertrophy of the walls of cerebral arterioles in stroke-prone spontaneously hypertensive rats. [37] PP was associated with prevalence and severity of cerebral white matter lesions in the ARIC (Atherosclerosis Risk in Communities) study. [38] One possible explanation for discrepancies between studies that have demonstrated the predictive value of brachial PP for cerebrovascular events and those that have not is that brachial PP, measured in both types of studies, may not reflect the effective PP acting at the site of the extra- and intra-cerebral circulation.

Indeed, brachial PP provides only an indirect estimate of aortic stiffness. [3] Because of the physiological amplification of PP between central and peripheral arteries, brachial PP may not reflect aortic PP. Boosting of aortic PP by reflected waves does not occur in the brachial artery, which means that amplification does not occur to the same extent in the central circulation (thoracic aorta, carotid arteries) and peripheral circulation (brachial artery). Moreover, factors other than aortic stiffness can influence the value of PP; these include heart rate, cardiac contractility, peak blood flow and venous
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pressure. Thus, it is conceivable that aortic stiffness could predict stroke events to a larger extent than brachial PP. In addition, as mentioned, measurement of aortic stiffness, which integrates changes in arterial walls, may also reflect parallel lesions present in the cerebral vasculature. Thus, arterial stiffness may be an ‘integrator’ of cerebrovascular atherosclerotic lesions, and a better predictor of stroke than PP.

3. Determination of Arterial Stiffness

Arterial stiffness can be assessed noninvasively by various methodologies, including pressure waveform analysis with tonometry, arterial diameter analysis with echotrackings systems, and stroke volume/PP ratio. Measurement of aortic pulse wave velocity (PWV) is generally accepted as the most simple, noninvasive, robust and reproducible method of detecting arterial stiffness.[39,40] PWV measured along the aortic and aorto-iliac pathway is of greatest clinical relevance because stiffness of the aorta and its first branches, which are elastic arteries in young healthy subjects, is responsible for most of the pathophysiological effects of arterial stiffness. PWV is usually measured using the foot-to-foot velocity method. Briefly, waveforms are obtained transcutaneously over the common carotid artery and the right femoral artery, and the time delay (t) is measured between the feet of the two waveforms. To simplify the method, the distance (D) covered by the waves corresponds to the distance measured between the two recording sites. However, it should be noted that this simplification overestimates PWV, since it introduces an additional distance, between the aortic valves and the carotid site. Other methods subtract the latter distance from the carotid-femoral distance.[40] The equation for calculating PWV is as follows: \( \text{PWV} = \frac{D}{t} \) (metres)/t (seconds).[40,41]

4. Predictive Value of Arterial Stiffness for Stroke

An indirect argument for an influence of arterial stiffness on the occurrence of stroke comes from cross-sectional studies showing that arterial stiffness and cardiovascular risk factors for atherosclerotic lesions are correlated. However, a major limitation of these studies is their cross-sectional nature.[4,42] These studies showed that aortic stiffness was associated with other markers of cardiovascular risk or the extent of atherosclerosis, but did not allow the conclusion that arterial stiffness was predictive of cardiovascular events because patients in these studies were not followed up over time. In other words, these studies showed that arterial stiffness was a marker of cardiovascular risk,[4,42] but did not demonstrate its predictive value as an intermediate endpoint.

Only recently, longitudinal studies have directly demonstrated that arterial stiffness, measured either from PWV,[17,43,44] carotid elastic modulus (a measure of carotid wall material stiffness)[45] or PP/stroke volume ratio[46] is an independent predictor of all-cause and cardiovascular mortality, in patients with uncomplicated essential hypertension[17,43] or end-stage renal disease.[44,45] In these studies, strokes were not analysed separately, but were included in the clinical endpoints (cardiovascular events and all-cause mortality).

In another recent longitudinal study,[47] we included 1715 patients with essential hypertension who had a measurement of arterial stiffness at entry (i.e. between the years 1980 and 2001) and no overt cardiovascular disease or symptoms. The mean follow-up was 7.9 years. Aortic stiffness was assessed at entry from the carotid-femoral PWV. A Cox proportional hazard regression model was used to estimate the relative risk (RR) of stroke and coronary deaths. In this population with a mean age of 51 ± 13 years, 25 fatal strokes and 35 fatal coronary events occurred. PWV significantly predicted the occurrence of stroke death in the whole population, with RR increasing by 1.72 (95% CI 1.48, 1.96;
p < 0.0001) for each standard deviation increase in PWV (4 m/sec) [table I]. Because most of the determinants of PWV, such as age and hypercholesterolemia, are also risk factors for stroke, it was necessary to verify that the predictive value of PWV on CHD events remained significant after adjustment for these risk factors. Importantly, the predictive value of PWV remained significant (RR = 1.39 [95% CI 1.08,1.72], p = 0.02) after full adjustment for classical cardiovascular risk factors, including age, gender, cholesterol level, diabetes, smoking, heart rate and MBP (table II). In this population, PP also significantly predicted stroke in univariate analysis, with an RR increase of 1.33 [95% CI 1.16, 1.51] for each 10mm Hg of PP, (p < 0.0001), but the relationship was no longer significant after adjustment for age (RR = 1.19 [95% CI 0.96, 1.47], p = 0.10). This study provided the first evidence, in a longitudinal design, that aortic stiffness is an independent predictor of fatal stroke in patients with essential hypertension.

The limitations of the current data should be recognised. First, further studies are required to assess the predictive value of arterial stiffness on non-fatal strokes in hypertensive patients. Secondly, these data need to be confirmed in a large population, because there are no data in the literature demonstrating simple univariate correlations between stroke and arterial stiffness. Whether these correlations exist after adjustment for age and/or blood pressure also needs to be considered. Thirdly, our conclusions are based on a small number of fatal strokes; further studies involving larger populations of hypertensive patients are required. However, as noted, the above study is the first longitudinal trial of its kind; numerous previous studies using a cross-sectional methodology have related arterial stiffness to the risk of stroke on the basis of risk equations but a case-control approach, but these were not based on longitudinal surveys.

5. Impact of Aortic Stiffness Reduction on Survival and Stroke

Although aortic stiffness is now well accepted as an intermediate endpoint for cardiovascular events (i.e. a significant longitudinal relationship between aortic stiffness and the occurrence of cardiovascular events has been demonstrated, independently of classical cardiovascular risk factors), its value as a surrogate endpoint for cardiovascular events has not been demonstrated until recently. Indeed, another major issue is to determine the impact of attenuation of aortic stiffness on survival, and particularly to demonstrate whether a reduction in PWV could predict a reduction in stroke independently of the normalisation of classical cardiovascular risk factors. Under these conditions, aortic stiffness may have a better predictive value than classical risk factors, since it integrates the damage of cardiovascular risk factors on the arterial wall over time. Indeed, BP, glycemia and lipids can be normalised in a few weeks using antihypertensive, antidiabetic and lipid-lowering drugs, with a consequent large reduction in cardiovascular risk factor scores. However, this is achieved without any improvement in atherosclerotic lesions or aortic stiffness, which requires a long-lasting correction of biochemical abnormalities. A discrepancy is thus expected between improvements in cardiovascular risk factors and persisting aortic stiffness.

Although a definitive answer to the question of the predictive value of aortic stiffness as a surrogate endpoint for cardiovascular events has not yet been obtained for the general population, Guerin et al. [48]...
have provided the first clear evidence in patients with end-stage renal failure (ESRF). These authors, who have previously shown that aortic PWV is a predictor of mortality in ESRF patients, evaluated the impact of aortic stiffness on all-cause and cardiovascular mortality as primary endpoints in this patient population. Because PWV is partly dependent on BP, and a decrease in BP can attenuate aortic stiffness (by reducing PWV), they tested the hypothesis that changes in PWV in response to decreases in BP could predict mortality in ESRF patients. In their study, 150 ESRF patients (mean age 52 years) were monitored for an average duration of 51 months. The changes in PWV in response to decreased BP were measured from entry until the end of follow-up. BP was controlled by adjustment of ‘dry weight’ and, when necessary, with ACE inhibitors, calcium channel antagonists, and/or β-adrenoceptor antagonists, used in combination if required. There were 59 deaths in the study group, of which 40 were due to cardiovascular causes and 19 to non-cardiovascular causes. Cox analyses demonstrated that independent of BP changes, absence of PWV decrease in response to BP decrease was a significant predictor of all-cause and cardiovascular mortality. After adjusting for all confounding factors, the risk ratios for absence of PWV decrease were 2.59 (95% CI 1.51, 4.43) for all-cause mortality and 2.35 (95% CI 1.23, 4.41) for cardiovascular mortality. These findings show that insensitivity of PWV to reduced BP is an independent predictor of mortality in ESRF patients. Thus, in this population, aortic stiffness is a good surrogate endpoint, i.e., its attenuation is predictive of reductions in all-cause and cardiovascular mortality.

It is important to note, however, that strokes and coronary events were not studied as separate endpoints in this study. Thus, the impact of attenuation of aortic stiffness on stroke remains to be established. Furthermore, because ESRF patients are at very high risk of cardiovascular events, the impact of aortic stiffness attenuation in other populations, including patients with normal (or mildly altered) renal function and those with cardiovascular risk factors such as hypertension, hypercholesterolaemia and diabetes, should be studied.

6. Therapeutic Implications for Stroke Prevention

Despite the lack of evidence that aortic stiffness attenuation is predictive of a reduction in stroke, recent data demonstrating the predictive value of aortic stiffness for stroke occurrence suggest that any drug able to reduce arterial stiffness should be useful in the treatment of patients at high risk of stroke. However, an important issue is whether drug treatment is able to prevent stroke by reducing arterial stiffness, independently of correction of cardiovascular risk factors, such as lowering BP. However, this question is somewhat theoretical, because the usual approach to stroke prevention in clinical practice is to attempt to reduce most cardiovascular risk factors, including hypertension, dyslipidaemia, diabetes and smoking, associated with arterial stiffening.

6.1 Antihypertensive Treatment

Antihypertensive treatment has been repeatedly shown to prevent cardiovascular events, including stroke. A meta-regression analysis across 27 clinical trials of antihypertensive drugs has demonstrated that reduction of high BP reduces both risk of death and morbidity from stroke, and that the level of protection achieved against stroke is related to the degree to which BP is reduced.

The authors of this meta-analysis claimed that these benefits of antihypertensive therapy on stroke occurred independently of the pharmacological class of antihypertensive agent used (i.e., β-adrenoceptor antagonists, diuretics, ACE inhibitors, angiotensin II receptor antagonists and calcium channel antagonists). In addition, the observed risk reduction in stroke in response to treatment-induced reduction in SBP was consistent with the risk reduction in stroke predicted from cohort study data. Taken together, these data suggest only a limited possibility of a pharmacological effect beyond BP reduction. However, it should be emphasised that our understanding of the overall effect of BP reduction is...
mainly drawn from meta-analyses and meta-regres-
sion analyses of intervention trials. This methodol-
gy can mask differences in stroke risk among popu-
lations, and differences in reduction of stroke risk
among different pharmacological classes. Interest-
ingly, despite these caveats, meta-analyses have
shown that stroke prevention in hypertensives may
be better achieved with calcium channel antagonists
than with diuretics or β-adrenoceptor antagonists.[52]

Studies of the effects of pharmacological agents
on arterial stiffness initially focused on hypertensive
patients because hypertension is the major cause of
increased arterial stiffness, both as a result of direct
BP-dependent effects and because of indirect ather-
ogenic mechanisms. As expected, numerous studies
have shown a decrease in arterial stiffness with use
of various pharmacological classes of antihyperten-
sive agents either acutely or during long-term stud-
ies.[53-61] Long-term studies (>3 months) are more
meaningful because hypertension is a chronic dis-
ease and acute effects, which can be opposed by
counter-regulatory mechanisms, may not predict
chronic efficacy.[59-61]

Repeate...
It seems likely that pharmacological treatment is able to improve arterial stiffness beyond BP reduction because long-term drug administration can modify the wall components, including a reduction in collagen density or changes in the spatial arrangement of wall materials. However, a BP-independent decrease in arterial stiffness of this type has not been unequivocally demonstrated during long-term treatment in individual studies involving hypertensive patients, particularly at the site of proximal elastic large arteries. Meta-analysis of individual data was necessary to show that the pressure-independent reduction in aortic stiffness (carotid-femoral PWV) after active treatment with ACE inhibitors, β-adrenoceptor antagonists, diuretics or calcium channel antagonists was observed only under chronic conditions, and not after acute treatment.

A pressure-independent decrease in arterial stiffness implies a pharmacological remodelling of the arterial wall. Indeed, various wall changes have been described in response to long-term antihypertensive treatment in animals. These include a reduction in collagen content and density, an increase in the elastin/collagen density ratio, a decrease in intima-media thickness, and changes in the connections of smooth muscle cells to extra-cellular matrix through fibronectin-integrins relationships. Furthermore, in clinical trials, remodelling of large arteries in response to long-term antihypertensive treatment has been noninvasively detected with ultrasound and reported to be characterised by a reduction in arterial lumen and intima-media thickness. Regression of arterial wall hypertrophy and reduction in arterial lumen were dependent on a reduction in local PP rather than on lowering of MBP. These findings emphasise the effects of cyclic stress on arterial remodelling, and the requirement to lower pulsatile stress through a decrease in arterial stiffness if significant pharmacological remodelling of large arteries is to be obtained. In contrast, in muscular arteries, a pressure-independent decrease in arterial stiffness may be observed after acute administration of an antihypertensive agent; this finding suggests an effect of smooth muscle relaxation on elastic and collagen elements at these sites.

In view of the important local actions of angiotensin II on arterial stiffening (fibrosis, collagen synthesis), drugs interfering with the RAAS are important candidates for reducing arterial stiffness. Indeed, recent data suggest pressure-independent effects of ACE inhibitors and aldosterone antagonists. A second potential group of interesting drugs is that of the nitrates/nitric oxide donors. There is now clear evidence that, within a certain dose range, this class of drugs can act relatively selectively on large arteries. This implies that these agents may potentially interfere with arterial stiffness without having marked effects on peripheral resistance. The newly developed dual inhibitors of neutral endopeptidase (NEP) and ACE are interesting molecules because they share the smooth muscle-relaxing effect of nitrates by increasing levels of intracellular cyclic guanosine monophosphate (cGMP) and inhibiting the effects of angiotensin II on the vessel wall.

6.3 Statins, Stroke and Arterial Stiffness

Although hypercholesterolaemia is an important modifiable risk factor for coronary events, it is not generally accepted as a risk factor for stroke. Although meta-analyses of statin trials in patients with CHD show that stroke events are reduced by statin agents, there is no clear evidence that this decrease in stroke events is due primarily to reduction in heart disease and subsequent cardio-embolic stroke events, or to some other mechanisms.

The effects of drugs on arterial stiffness have been much less studied in hypercholesterolaemic patients than in hypertensives. In patients with familial hypercholesterolaemia and hypertension, arterial stiffness was reduced considerably after 2 years’ treatment with simvastatin, whereas no significant change was observed after only 6 months’ treatment. Other studies using short-term treatments did not show any significant improvement. This indicates that the time needed to improve arterial stiffness in hypercholesterolaemic patients can be extremely long.
The non-lipid-lowering effects of statins are of great interest for improving arterial stiffness. Indeed, statins\(^\text{[2,84]}\) may upgrade endothelial nitric oxide synthase (eNOS), inhibit inducible NOS, attenuate the inflammatory cytokine responses that accompany tissue ischemia, and possess antioxidant properties that ameliorate ischemic oxidative stress in target organs.\(^\text{[2,79-84]}\) Other major beneficial pleiotropic effects of statins include modification of endothelial function, inflammatory responses, plaque vulnerability, and thrombus formation.\(^\text{[2,79-84]}\)

There is an urgent need for clinical trials that define in terms of outcomes (fatal and non-fatal stroke) whether reduction in arterial stiffness with statins is a desirable therapeutic goal. In this context, large artery properties may provide surrogate endpoints that are more useful than mortality and morbidity endpoints for assessing the effects of therapeutic interventions on cardiovascular risk.

6.4 Other Mechanisms for Reducing Arterial Stiffness

A promising therapeutic strategy for reducing arterial stiffness is direct targeting of the molecular events leading to arterial stiffening. Advanced glycation end products (AGEs) are responsible for the arterial stiffening in conditions such as diabetes\(^\text{[85]}\) and aging\(^\text{[86]}\) in animal models. Drugs interfering with the formation of AGEs, such as aminoguanidine (pimagedine) and ALT-711 (alagebrum chloride), have been shown in animal models to reverse arterial stiffening without influencing BP.\(^\text{[87,88]}\) ALT-711 has also been shown to improve total arterial compliance in aged humans with vascular stiffening.\(^\text{[88]}\)

7. Conclusion

Assessment of aortic stiffness may help to identify patients at high risk of stroke and allow more effective targeting of interventions. A growing body of evidence suggests that aortic stiffness is an independent predictor of stroke, and that aortic stiffness attenuation has an impact on survival. More longitudinal studies are needed to confirm the predictive value of aortic stiffness on primary and secondary events, in low- and high-risk populations and in various countries, using different methodologies of arterial stiffness measurement.

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