

Antihypertensive agents and arterial stiffness

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Carotid-femoral pulse wave velocity (cfPWV) is the gold-standard method to measure arterial stiffness (1), which has been shown to be an important predictor of cardiovascular events and death (1-3). A previous systematic review observed that each 1 m/s increase in pulse wave velocity (PWV) was related to 10% higher risk of cardiovascular events (2). In addition, a recent meta-analysis showed that PWV was able to predict future cardiovascular events and to improve risk classification after adjusting for other established risk factors (4). Identification of arterial stiffness may be particularly useful in intermediate cardiovascular risk patients as an adjunct to standard models of risk stratification (4).

According to some authors, augmentation index (AIx) is also a predictor of cardiovascular events (2). A previous meta-analysis showed that each 10% increase in AIx was related to 32% higher cardiovascular risk (2). Besides, a recent cohort study demonstrated that AIx was a predictor of cardiovascular events and mortality, especially in men (5). However, AIx is not a direct stiffness parameter, but the result of the interaction between several factors (1). Blood pressure (BP) and heart rate are two of the most important variables that influence AIx.

A recent analysis of the Framingham Heart Study showed that cfPWV was a predictor of incident hypertension in a 7-year follow up (6). Moreover, high BP at baseline was not associated to progressive arterial stiffening. These data suggest that arterial stiffness may be a cause and not a consequence of hypertension (1,6). Arterial stiffness is directly related to age and BP, and most antihypertensive drugs can attenuate this process of vascular aging (7). However, there is still controversy whether the stiffness regression mechanism is by lowering BP or if there is a

direct drug effect on the arterial wall. In addition, there may be differences regarding stiffness regression among antihypertensive drug classes.

In a recent issue of this journal, Chen *et al.* conducted a systematic review to compare the effects of angiotensin receptor blockers (ARB) and other classes of antihypertensive drugs in improving arterial stiffness of hypertensive patients (8). The authors were particularly careful to include only randomized controlled trials. They observed that ARBs were superior to other antihypertensive drugs in reducing AIx but not PWV. The authors hypothesized that heart rate differences, heterogeneity of patients and insufficient statistical power could justify their results.

We recently published a head-to-head study between an angiotensin converting enzyme inhibitor (ACEi) and an ARB showing similar effects on PWV and AIx (9). In a narrative review, Liu *et al.* observed that ACEi and ARB might be more efficacious than other antihypertensive classes in reducing arterial stiffness (7). In addition, beta blockers were inferior in reducing AIx, and the authors attributed this effect to the reduction of heart rate (7). In a previous meta-analysis, Shahin *et al.* demonstrated that ACEi were superior to placebo in both PWV and AIx reduction (10). However, ACEi and ARB effects were similar as well as the comparison between ACEi and other antihypertensive agents. Specific mechanisms of action of ACEi and ARB may justify their relative superiority to attenuate arterial stiffness, as these drugs are related to improvement of endothelial dysfunction, reduction of large artery wall thickening and regression of smooth muscle cell hypertrophy (11). Important studies limitations in those meta-analyses were small sample size, short follow-up period and lack of cardiovascular events analysis.

BP reduction remains the cornerstone of the antihypertensive therapy. At the present time, calcium channel blockers, ACEi, ARB and thiazide-like diuretic are all first choice treatments for hypertension. However, other effects beyond BP reduction may lead to their compelling indication in some situations. Arterial stiffness is a powerful predictor of cardiovascular events and may be a precursor of hypertension and atherosclerosis. Therefore, antihypertensive drugs that improve arterial stiffness may be a reasonable choice in hypertension treatment. Drugs that inhibit the renin-angiotensin-aldosterone system seem to be superior to other antihypertensive drugs in reducing arterial stiffness.

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Footnote

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Comment on: Chen X, Huang B, Liu M, *et al.* Effects of different types of antihypertensive agents on arterial stiffness: a systematic review and meta-analysis of randomized controlled trials. *J Thorac Dis* 2015;7:2339-47.

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