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Editorial

Do We Have Effective Means to Treat Arterial Stiffness and High Central Aortic Blood Pressure in Patients with and without Hypertension?

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The reduction or loss of arterial elasticity or distensibility leads to arterial stiffness (AS), which has a substantial predictive value for all-cause and cardiovascular disease (CVD) mortality, as well as for non-fatal CVD events [1]. A plethora of evidence consistently showed the prognostic value of aortic stiffness for fatal and nonfatal CVD events in various populations at different levels of CVD risk, including the general population, elderly subjects and patients with hypertension, type 2 diabetes mellitus (T2DM) and end-stage renal disease (ESRD) [2]. It has been reported that 1-SD increase in pulse wave velocity (PWV) is associated with a 47% increase in the risk for total mortality [95% confidence interval (CI), 1.31-1.64] and a similar 47% increase in the risk for CVD mortality (95% CI, 1.29-1.66) [2].

Age is the major CVD risk factor and this is attributable in part to stiffening of large elastic arteries, a natural process [3]. During aging, the elastic lamella grows to be fragmented and the mechanical load is transferred to collagen fibers, which are several hundred times stiffer than elastic fibers. This loss of the elastic properties (AS) mainly happens with large arteries and causes arteriosclerosis different than atherosclerosis, which refers to the arterial intima [4]. Arteriosclerosis usually does not affect the smaller muscular arteries [5]. Besides age, a number of changes in arterial wall, related to CVD risk factors, also increase AS and contribute to early arterial aging [3]. Matrix remodelling of the media and adventitia may result from endothelial dysfunction, reduction of elastin, increase of collagen metalloproteinases, vascular smooth muscle cells and adhesion molecules, and deposition of advanced glycation end-products and calcium due to low-grade inflammation, dyslipidaemia, T2DM, hypertension (HTN) and chronic kidney disease (CKD) [3]. Arterial stiffness increases PWV; this causes an early return of the reflection wave in the aorta during left ventricular systole [6]. This early return increases central aortic pressure and systolic blood pressure, while it reduces diastolic blood pressure 2/6 and thus coronary perfusion [6]. Central aortic pressure is only an indirect, surrogate measure of AS. However, it provides additional information concerning wave reflections [6,7]. Central pulse-wave analysis should be optimally used in combination with the measurement of aortic PWV value to determine the contribution of AS to wave reflections [6,7]. Given the complex pathogenesis of AS, it is obvious that the treatment of AS should also be multifactorial. Both lifestyle and pharmacological approaches should be implemented in these patients. Central pulse-wave analysis should be optimally used in combination with the measurement of aortic PWV value to determine the contribution of AS to wave reflections [6,7]. Given the complex pathogenesis of AS, it is obvious that the treatment of AS should also be multifactorial. Both lifestyle and pharmacological approaches should be implemented in these patients. Increased leisure time physical activity, weight reduction, avoidance of diatery salt and alcohol abuse as well as increased consumption of diatery heavy chain omega fatty acids as recommended [7]. Drug treatment for arterial hypertension [diuretics, angiotensin-converting enzyme inhibitors (ACE-I), angiotensin-receptor blockers (ARBs), and calcium-channel blockers (CCB)] [8-10]; lipid-lowering agents, mainly statins [11,12], hypoglecaemic drugs (thiazolidinediones) [13]; and potentially other novel agents, including AGE breakers [14]. There are been data suggesting that the reduction in AS during treatment for arterial hypertension is not only attributed to the reduction in BP per se but to additional BP lowering-independent effects of antihypertensive drugs [15]. Indeed, the renin – aldosterone - angiotensin –system (RAAS) blockers, ACE inhibitors and ARBs, have been shown to have a BP- independent beneficial effect on AS [16] and to possess antifibrotic effects [17].

In antithesis, β-blockers do not reduce AS in the same degree, because non-vasodilating β-blockers are less effective in reducing central pulse pressure than other antihypertensive drugs [7]. In fact, older β-blockers may increase vasoconstriction and assist the early return of the reflected pulse wave in late systole (and not in diastole),

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thus increasing central blood pressure and inducing a mismatch between the heart and the arterial system [7].

The substudy of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) [18], Conduit Artery Function Evaluation (CAFE) trial [19], showed that amlodipine combined with perindopril reduce central aortic pressure more than atenolol 3/6 combined with thiazide despite a similar impact on brachial BP. Moreover, central aortic pulse pressure may be a determinant of clinical outcomes, and differences in central aortic pressures may be a potential mechanism to explain the different clinical outcomes between the latter treatment arms in ASCOT [19]. In conclusion, even AS increases with age, this process might be accelerated by the simultaneous presence of other CVD risk factors, resulting in early vascular aging. AS is associated with increased risk for CVD and all-cause mortality, and it is possible that a decrease in AS might improve outcomes. Various approaches, particularly those targeting HTN, T2DM, dyslipidaemia, metabolic syndrome and CKD, preferably combined in a multifactorial approach, contribute to reduction in AS. In addition, the potential role of newer therapies, including AGE breakers and those aiming to break collagen cross-links, should be tested.

CONFLICT OF INTEREST

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