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EDITORIAL COMMENT

Aortic Stiffness Matters: Ventricular-Arterial Interactions Over Time*

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Vascular-ventricular interactions constitute an important element of our dynamic cardiovascular circulation. In this regard, ideal coupling of the left ventricle (LV) and systemic arterial system promotes optimal cardiac output and blood pressure. It is well known that the aorta increases in stiffness with increasing age as well as in association with other cardiovascular risk factors. Arterial/aortic stiffness is itself an independent risk factor for cardiovascular events (1). Furthermore, arterial stiffness can become a major therapeutic issue in conditions such as heart failure, as well as in conditions in which there are additional increases in impedance/resistance to LV output—for example, in severe aortic stenosis. In selecting medication for treatment of heart failure, the physician must keep in mind the effect of systemic arterial stiffness on LV pump function. Similarly, aortic valve replacement may not provide the desired degree of symptomatic and prognostic improvement in an aortic stenosis patient in whom aortic stiffness/resistance has not been optimized. Consequently, aortic/arterial stiffness and ventricular-arterial coupling are important prognostic and therapeutic concepts.

It is in this context that in this issue of *iJACC*, Cauwenberghs et al. (2) evaluate to what extent central arterial pulse pressure (cPP) and carotid-femoral pulse wave velocity (PWV) measured at baseline, and again after 4.7 years (mean), are associated with changes in LV anatomy—relative wall thickness and mass—and a number of measures of LV diastolic function in a family-based, northern Belgian population sample of FLEMENGHO (Flemish Study on Environment, Genes, and Health Outcomes). From 1985 to 2005, the authors recruited 607 participants (50% women, mean age 51 years) and studied them using transthoracic echocardiography, as well as applanation tonometry of the carotid, femoral, and brachial arteries to assess cPP, PWV, and the augmentation pressure (AP) index (**Figure 1**). Major findings of this study include that after adjustment for traditional risk factors in both men and women, longitudinal (over time) increases in ventricular septal and posterior wall thickness in the range of 12% to 14%, and decreases in LV internal diameter in the range of approximately 12%, were associated with higher baseline PWV. This resulted in greater increases in relative wall thickness with higher baseline PWV. In addition, patients with higher baseline PWV were at greater risk (odds ratio 1.35) for developing or maintaining LV concentric remodeling geometry—defined as a relative wall thickness >0.42. Importantly, LV concentric remodeling has been associated with an increased risk of cardiovascular outcomes (3). Of additional interest, the authors noted sex differences in the relation of aortic stiffness parameters and LV measurements. In particular, in women, but not in men, higher baseline cPP was associated with a longitudinal increase in LV mass and E/e' ratio—the latter parameter reflecting 1 element of worsening LV diastolic function, namely, a probable increase in left atrial pressure. Furthermore, a greater longitudinal increase in cPP was independently related to decreases in factors reflecting LV diastolic function—that is, transmitral E wave, e' velocity, and transmitral E/A ratio—in women, but not men. The authors found no significant association between longitudinal changes in LV structural indices and change in PWV in either men or women.

This paper demonstrates some notable strengths and weaknesses. Among its strengths, it extends previous observations on the relationship of LV mass,

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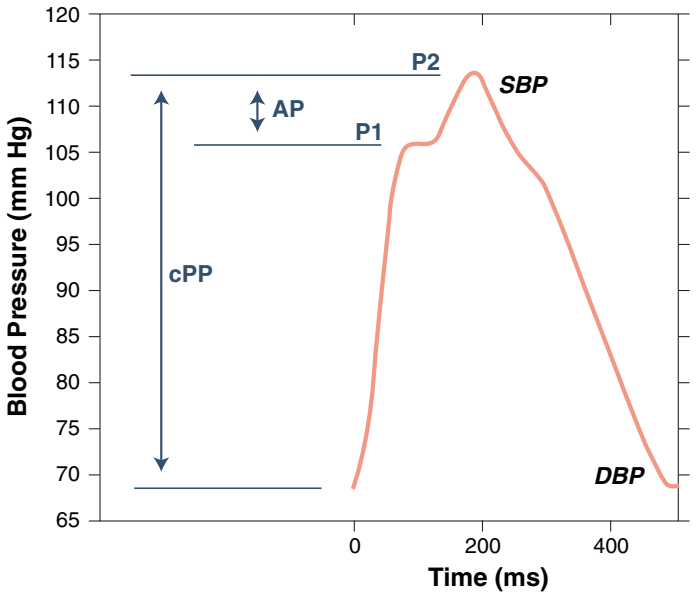
FIGURE 1 Diagram of Aortic Pressure Curve



The curve shows central arterial pulse pressure (cPP), systolic (SBP), and diastolic (DBP) blood pressures, and augmentation pressure (AP), where AP = P2 - P1. Carotid-femoral pulse wave velocity is calculated by dividing the distance between the 2 arteries by the transit time between them. (Modified from Piskorski et al. Int J Cardiol 2013;168: 2899–900; used with permission.)

geometry, and diastolic function to arterial stiffness by providing longitudinal data regarding the relationships of these parameters over a 5-year period in a well-characterized, family-based population sample. In addition, the sex differences described in this paper are of interest. The authors suggest that the sex-dependent relations between LV diastolic function and cPP noted might be explained by the higher aortic stiffness and pulsatile hemodynamic load previously reported in women compared with men. Coutinho et al. (4) reported in a study of non-Hispanic whites from the GENOA (Genetic Epidemiology Network of Arteriopathy) study that proximal aortic stiffness was greater in women than men and was associated with LV diastolic dysfunction. They postulated that women may be more susceptible to the deleterious effects of greater pulsatile and early arterial load on diastolic function and ventricular-arterial interaction and suggested that this may contribute to the greater risk of heart failure with preserved ejection fraction (HFpEF) in women, previously reported to outnumber men with HFpEF by a 2:1 ratio. Another strength of the current study is the fact that baseline and follow-up echocardiographic studies were all read by a single experienced reader.

Study limitations include the fact that, as the authors note, only white European participants were included. In addition, only 60% of those invited to participate actually had follow-up studies performed—for a variety of reasons. As a physician with long-standing involvement in echocardiographic evaluations of large populations, I feel compelled to comment on additional elements of the echocardiographic design that would benefit from enhancement. First, since, as the authors note, their echocardiographic studies were digitally stored, they would do well to measure—if they have not already done so—other important components reflecting LV diastolic function, including left atrial volume index and tricuspid regurgitation jet velocity, as outlined in recent guidelines from the American Society of Echocardiography and the European Association of Cardiovascular Imaging (5). Similarly, the authors would do well to measure strain—at least global longitudinal strain—from the digitally stored images because global longitudinal strain has been shown to be an early marker of LV dysfunction. In addition, although it is laudable that a single experienced reader interpreted the echocardiographic studies—thus eliminating the concern for inter-reader measurement variability—another concern (unless the baseline and follow-up studies were both measured at the same time) is whether there was any temporal drift in the approach used by the reader to make measurements from the studies performed at baseline and nearly 5 years later (6).

Hemodynamics in the aorta change with advancing age such that after approximately 55 years of age, cPP and systolic blood pressure tend to increase dramatically, whereas the AP plateaus and then decreases (1). Mitchell (1) suggests that stiffening of the aorta with advancing age is generally associated with minimal change or even a reduction in stiffness in the peripheral muscular arteries, leading to a reduction and reversal of the normal centrifugal arterial stiffness gradient. By middle age, a moderate increase in PWV leads to early arrival of the reflected wave and increased overlap between forward and reflected pressure waves. Loss of this proximal reflecting site with aging may explain why the AP decreases with advancing age at a time when pulse pressure increases noticeably. These findings suggest, according to Mitchell (1), that proximal aortic stiffening and increased forward pressure wave amplitude, rather than increased wave reflection, account for the marked increase in cPP with advancing age. Forward wave amplitude and PWV are similarly dependent on aortic wall stiffness, whereas forward wave amplitude, the predominant determinant of cPP, is more

sensitive to alterations of aortic diameter. Importantly, these related, but disparate, measures of arterial stiffness contribute separately to the adverse effects of arterial stiffening on LV anatomy and function.

The authors are to be commended for extending our understanding of ventricular-arterial interactions over time in a population-based study and highlighting sex differences that may help explain the disproportionate prevalence of HFpEF in women. Their study focuses our attention on the often-ignored importance of ventricular-arterial interactions and the fact that arterial stiffness matters.

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