Stiff Arteries, Stiff Ventricles: Correlation or Causality in Heart Failure?

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The biophysical properties and neurohormonal regulation of arterial function are influential mediators of cardiovascular disease. Over the past 3 decades, the prognostic importance of arterial stiffness, as a measurable indicator of arterial function, has been recognized in both unselected populations and among patients with cardiovascular risk factors. Although there is a correlation between vascular stiffness and outcomes, the temporal and causal interrelationships with aging, hypertension, atherosclerosis, and the progression to heart failure are not fully understood. Aortic stiffening increases systolic load on the left ventricle (LV) contributing to ventricular hypertrophy and leading to increased myocardial oxygen demand, as well as indirectly promoting coronary disease and impaired perfusion. Arterial stiffness and wave reflection effects augment systemic blood pressure and place additional mechanical load on the heart leading to diastolic dysfunction and myocardial fibrosis. Increasing vascular stiffness precedes the onset of hypertension and may promote alterations in wall stress that accelerates atherosclerosis. This body of evidence has generated renewed interest in discovering whether arterial stiffness is more than a correlated risk factor and if it could play a role in the causative pathway to adverse cardiovascular events.

See Article by Ohyama et al

The proximal elastic arteries serve as capacitance vessels that distend to accommodate the stroke volume as it is transferred from the heart to the circulation and maintain efficient coupling with the mechanical properties of the myocardium. During systole, a pulse wave is propagated along the aorta that travels at a velocity that is an accurate surrogate for arterial stiffness. With advancing age, elastin fibers in the tunica media become degraded and fragmented leading to a less compliant collagen-dominant state with an associated rise in pulse wave velocity (PWV) and reflected pressure waves. Endothelial dysfunction plays a pivotal role in the progression to heart failure with neurohormonal interactions between the myocardium and the endothelium driving unfavorable outcomes. Genetic factors are also influential but, although the heritability of carotid-femoral PWV is ~40%, the genetic variants that independently influence vascular stiffness are not well defined. An important unanswered question in cardiovascular medicine is what role aortic stiffness may play in the initiation of myocardial dysfunction and subsequent progression to heart failure in the general population.

In this issue of Circulation: Cardiovascular Imaging, Ohyama et al explored the relationship between aortic PWV and LV function using phase contrast imaging and strain analysis of tagged cardiac magnetic resonance imaging in a large multiethnic cohort. Age-related changes in proximal aortic stiffness have previously been associated with LV mass and concentricity independent of central blood pressure and conventional cardiovascular risk factors. New data of Ohyama et al indicate that higher aortic arch PWV is also associated with impaired circumferential systolic strain and diastolic function in a community-based population. This study provides further evidence implicating aortic stiffness in adverse cardiac remodeling and impaired myocardial function. A previous longitudinal Multi-Ethnic Study of Atherosclerosis (MESA) study investigated 5960 participants using radial artery tonometry and found that the magnitude of wave reflections was strongly predictive of new-onset heart failure, but did not assess PWV itself. It has been argued that systolic load ultimately determines LV remodeling, and the indirect effects of aortic mechanical properties are of secondary importance, but measures of aortic stiffness are also relatively less confounded by the degree of LV dysfunction. A Framingham cohort study of 2539 middle-aged to elderly adults followed up for a median of 10.1 years reported that carotid-femoral PWV was associated with an increased risk of incident heart failure—and comparable risk was conferred by PWV in patients with heart failure with either preserved or reduced ejection fraction. These data would suggest that, as there is no treatment for heart failure with preserved ejection fraction of proven benefit, modulating vascular function may be a promising target for intervention.

Recent observational longitudinal data, also from the same MESA investigators, suggest that blood pressure control may be effective in halting the progression of aortic stiffening and breaking the vicious circle between hypertension and vascular aging. Measurement of aortic wall stiffness could provide a sensitive indicator for the initiation of vascular disease, but interventional studies have yet to determine whether a lowering of PWV leads to a reduction in cardiovascular events independent of alterations to classical risk factors. Endothelial cells are mechanosensitive and directly respond to stiffening of the extracellular matrix leading to enhanced permeability.
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References

None.


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