A revered senior colleague once said to me on my birthday, “Aging beats the alternative.” As the proportion of older adults among the world’s populations continues to increase, health assessment in “middle age” becomes increasingly important. Present guidelines from the American Heart Association with the American College of Cardiology recommend a global assessment of risk to prevent or delay the onset of chronic disease. The assessment, though global, is primarily focused on evaluations of systemic vasculature and associated risks for cardiovascular morbidity and mortality. Preventive measures entail many items typically addressed in this journal: education for a healthy lifestyle and routine physician visits to check systemic blood pressure, calculate body-mass index, measure waist/hip ratio, and perform laboratory testing with a fasting lipid panel. Each of these elements is linked to prognosis for long-term cardiovascular health, including isolated systolic hypertension. Prevention of ischemic and nonischemic complications associated with systemic hypertension through lifestyle interventions and the administration of antihypertensive therapeutics available for oral everyday use has improved cardiovascular health, reducing early morbidity and mortality.

These gains have been based on the ease and reproducibility of measurement of systemic blood pressure by healthcare providers through techniques first reported over a little more than 100 years ago. During this past century, evaluation of an important “loop” in circulation, the pulmonary vasculature, has played no role in preventive medicine. The obvious reason is that no noninvasive equivalent to sphygmomanometry and its digital successors has been available for pulmonary vasculature pressures. Invasive cardiac catheterization is still the gold standard.

In the current issue of Circulation, Lam and colleagues report initial findings of a massive effort to use echocardiographic measurements of pulmonary artery systolic pressure (PASP) to begin to make up for the lost time relative to the epidemiology of systemic blood pressure. Using the resources of the Rochester Epidemiology Project (1997 to 2000), a random sample of the Olmsted County, Minn, population aged ≥45 years, the investigators compared the measured pressures in the systemic (by blood pressure cuff) and pulmonary vascular circulations (by echocardiography) to determine if PASP independently predicted mortality. To use standard calculation methods the investigators only included echocardiograms from the 1413 out of 2042 participants who had analyzable tricuspid regurgitation (TR) jets. A technique to increase the number of analyzable TR jets, enhancement with agitated saline, was not performed. Measurements were performed in careful fashion with all images collected by 1 of 3 cardiac sonographers and interpreted by an echocardiologist (Dr Margaret Redfield) who was blinded to the clinical data. Compared with other participants, the subjects with analyzable TR jets were older, more frequently women, had a lower body-mass index and less comorbid disease. The presence of coronary artery disease and heart failure did not differ between those with and without TR jets. Subjects’ ages ranged from 45 to 96 years old.

This is the first cross-sectional population-based evidence of age-associated increase in pulmonary artery pressures and all-cause mortality independent of age and clinically apparent cardiovascular disease. The investigators analyzed the entire population and the population without known cardiovascular disease separately. Surprisingly, the 2 populations had the same median PASP, 26 mm Hg (interquartile range 24, 30). This range of pressures is obviously more compressed than for systemic pressures, and the relationship between increments in that pressure with advancing age is also compressed. The absolute value is similar to recent reports of normal patients referred for echocardiography, 28±5 mm Hg, (mean; range 15 to 57) which is reassuring. The problem with small changes in echocardiographic estimates of PASP is that unlike systemic blood pressure, which has a wide variance in the population, it appears that this variance in PASP is smaller and the technique is more dependent on the skills of the technicians and the technology and the patient’s body habitus and comorbid disease (eg, lung disease). To discriminate patients at risk effectively from those who aren’t is much more challenging. On a population basis, small differences of 1 to 4 mm in PASP have a big impact on mortality. How to measure these subtle changes reliably in the individual is not known.

Is the minor elevation in PASP an early indicator of left ventricular diastolic abnormalities? As with plumbing, an elevated pressure downstream that is transmitted backward eventually “clogs” the system. A common cause of elevated pulmonary pressures, increased left heart filling pressures, elevates pulmonary pressures by backward transmission,
ultimately resulting in biventricular failure. This occurs because, unlike the systemic circulation where downstream pressure is low compared with the arterial pressure, pulmonary venous pressure is quite high and thus similar to the arterial pressure. The first presentation of this elevated pressure is usually diastolic relaxation abnormalities producing pulmonary edema. This may be increasing from an epidemiological standpoint because of age-related left ventricular diastolic dysfunction.

The incidence of heart failure resulting from abnormalities of diastolic dysfunction with normal systolic function (heart failure with a normal ejection fraction) has increased to >50% of heart failure patients overall and has an overall survival only slightly better than heart failure patients with reduced systolic function. The investigators of this study hypothesized that elevation of PASP may correlate with measures of left ventricular compliance. All measures associated with this compliance, including systemic arterial pulse pressure (a measure of systemic vascular stiffness), a tissue Doppler parameter estimating left ventricular diastolic pressure (E/e'), and left atrial volume, associated with a continuous increase in PASP without significant sex-related differences or correlations with body-mass index after adjustment for age. Elevated PASP may be an indicator of early diastolic abnormalities.

Before the appearance of this report, most of what we knew about pulmonary vasculature changes with age had been from examination of pathology specimens. The pulmonary trunk is more extensible than the aorta, and extensibility declines with age. The pulmonary arterial vasculature develops increased medial thickness, with some studies finding diminished elastic tissue and increased collagen and others finding no change in elastin and decreased collagen stiffening the vessels. Intrapulmonary vascular ultrasound is not yet sufficiently developed to examine the distribution of these constituents in vivo. But, noninvasively, echocardiography can measure the estimated PASP. The significance of these pathological changes and how they correlate with pressure, the rate of progression, the population at risk, and the ability to predict outcomes are unclear.

It is important to classify patients with elevated pulmonary pressures properly. Myriad diseases with variable treatments and prognoses have pulmonary hypertension as the primary or concomitant manifestation, and the underlying cause of the pulmonary hypertension determines treatment and prognosis. For pulmonary vascular disease, patients often present to tertiary centers with advanced disease, given that symptoms tend to develop only after right ventricular function is severely impaired because of the increased afterload. Although idiopathic/heritable (previously known as "primary") pulmonary arterial hypertension is a rare disease, pulmonary hypertension is associated with many more common conditions such as connective tissue diseases, congenital heart disease, liver disease, and human immunodeficiency virus. Early detection in the general population by echocardiography may help identify patients at risk before irreparable damage occurs.

What is the value of this information? The faults of the study lie with the reproducibility and generalizability of PASP measurement by echocardiography. Identified on a population basis, the measurement differences and the reliability of any center’s ability to discriminate this closely even just 1 mm Hg is hard to imagine. Systemic blood pressure likely faced the same criticisms, which is why recommendations have specific cutoff points with repeated measures. The difference is that only 69% of subjects had interpretable TR jets (although injected saline was not used) and all subjects had reliable systemic blood pressure readings. Without knowing the intraobserver variability, these small differences may be within the variance. The authors did not collect key routine measures used in the evaluation of elevated pulmonary pressures, such as right ventricular function, even though in the general population with mild elevations of PASP, dysfunction is unexpected. Pulse oximetry and the diffusion capacity of carbon monoxide would have been a valuable measure of intrinsic pulmonary (also not collected by history or diagnostic testing) and pulmonary vascular disease.

What are the implications of these data and what are the important next steps for developing these measurements for more practical use? It appears that PASP increases with age in this population and now needs to be studied in a more heterogeneous population to determine if race affects the level of elevation. A relatively low PASP of 24 to 28 mm Hg, often overlooked in a normal subject, appears to be a significant level for increased mortality (especially over 28 mm Hg). These values are only slightly higher in subjects with known cardiovascular disease. It may be reasonable to apply these data now with this point in mind, that what may have been considered a trivial elevation is not trivial. It appears to be a marker of early diastolic abnormalities and could be used as a signal to more aggressively treat risk factors, promote lifestyle changes, or address concomitant cardiovascular disease. But only age and PASP remained independent risk factors for mortality after exclusion of cardiopulmonary disease, implying that PASP may not just be a reflection of arterial stiffening, diastolic abnormalities, or concomitant disease but a new independent risk factor. More data are needed, but it is possible that echocardiography could potentially be a routine screen if prevention studies prove successful. PASP may be a new, uncovered, previously silent risk.

Disclosures
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References


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