Normal left ventricular function consists of 2 interrelated processes. Systole comprises a coordinated interplay between fiber shortening, wall thickening, longitudinal shortening, and cardiac twist, which results in the generation of stroke volume. During diastole, which comprises relaxation and untwist, as well as contraction of the atrium, the normal ventricle relaxes and fills to an adequate end-diastolic volume at low pressure—thus optimizing stroke volume in the next systole.

The noninvasive assessment of systolic and diastolic function is a major undertaking of cardiologists, and in 2015, this assessment is usually performed with echocardiography. The assessment of systolic function, which began with M-mode echocardiography in the 1970s, now comprises both 2D and 3D echocardiography, as well as regional function assessment with speckle tracking. The assessment of diastolic function became routine in the 1980s, with the development of pulsed Doppler measurement of transmitral flow velocities: early (E) and late/atrial contraction (A) velocities and pulmonary venous flows.

We think that there are 2 principal justifications for this time and trouble. First, the assessment of filling pressures can guide clinical decision-making. The second is underscored by the findings of Kuznetsova et al in the current issue of Circulation: Cardiovascular Imaging. Diastolic function grading, along with other echocardiography data about structure and function, can be adapted for use in large epidemiological survey. We are learning from these studies how diastolic function evolves over time and how these changes are related to the development of heart failure.

One of the first observations linking the E/A ratio and outcome came from the Cardiovascular Health Study and the Strong Heart Study, which showed that the extremes of this ratio predicted incident heart failure. The study that put echo-epidemiology on the map, in our opinion, was performed by Redfield and coworkers. These investigators applied a comprehensive scheme for grading diastolic function, including tissue Doppler, in the prospective cross-sectional assessment of 2042 citizens of Olmstead County, Minnesota, of mean age 62.8 years. The prevalence of various forms of diastolic dysfunction was mild (21%); moderate (7%); and severe (1%). Thus, most diastolic dysfunction in the community was mild, implying normal resting filling pressures, and was asymptomatic: this was true even among most of the population who had reduced (<40%) ejection fraction. The prevalence of all types of diastolic dysfunction increased with age and was more prevalent among patients with diabetes mellitus, hypertension, and coronary heart disease.

This work also gave us insight into the relationship between systolic and diastolic dysfunction: almost 80% of subjects with ejection fraction <50%, the usual cutoff for normal ejection fraction, had concomitant diastolic dysfunction, suggesting that the notion that ventricular dysfunction is purely systolic or purely diastolic is overly simplistic. Finally, using multivariate models which controlled for age, ejection fraction, and other factors, the authors showed that the severity of diastolic dysfunction was directly related to all-cause mortality.

In the present study, Kuznetsova and coworkers measured transmitral and tissue Doppler variables in 650 participants (mean age 50.7 years) at baseline and after 4.7 years in FLEMENGO (Flemish Study on Environment, Genes, and Health Outcomes) participants from a geographically defined region of Belgium. In this population, the prevalence of diastolic dysfunction was 25%, not dissimilar to the frequency observed in Olmstead County. Over the period of observation, diastolic dysfunction grade remained unchanged in 87.2%, improved in 3.7%, and worsened in 9.1%. Baseline age was a strong predictor of worsening of diastolic dysfunction from normal/mild grade to a more advanced grade. A doubling of baseline insulin was associated with a 184%
increase in the odds of worsening of diastolic function grade. Moreover, baseline diastolic BP and the change in systolic BP over time predicted worsening of diastolic dysfunction. It should be noted that these data "echo" findings of Kane et al who performed a similar serial study on the older Olmstead County cohort and showed a near doubling in the prevalence of diastolic dysfunction, a worsening of diastolic function in 23%, and a similar relationship of worsening diastolic function to age.\(^9\)\(^10\)

These echo-epidemiology surveys make some important contributions. First, we now have a sense of how diastolic function parameters evolve over time. Second, we have a link between baseline diastolic dysfunction and worsening of diastolic dysfunction and the development of heart failure.\(^8\)\(^9\)\(^10\)

Diastolic dysfunction\(^10\) and, specifically, tissue Doppler \(e’\) is an independent predictor of heart failure events after adjustment for age and hypertension;\(^13\) the incidence of heart failure and other outcomes vary directly with the severity of diastolic dysfunction.\(^15\)

There data contain implications for the prevention of heart failure. The authors have found a striking increase in the development of diastolic dysfunction over time in subjects whose insulin levels doubled during the study period. These findings reflect the recent finding that hyperinsulinemia, in patients without diabetes mellitus, correlates with subtle abnormalities in diastolic function.\(^15\)\(^16\) In many studies, this correlation is independent of body mass index or left ventricular hypertrophy. Whether insulin resistance in the heart is mediator or a marker of disease is still not known.\(^17\) Mechanical abnormalities may be the result of a myocardial substrate switch from preferential use of fatty acids to carbohydrate in the face of excess metabolic load. Hyperinsulinemia may also result in expansion of the cardiac extracellular matrix or reductions in aortic distensibility; both of which could alter myocardial mechanics. Irrespective of the mechanism, it is clear that serum insulin is an early marker of metabolic disease that is likely mirrored in impaired myocardial relaxation.

Second, this work underscores the relationship between hypertension, the development of diastolic dysfunction, and incident diastolic heart failure. We have known for some time that diastolic dysfunction is highly prevalent among patients enrolled in hypertension clinical trials; In LIFE (Losartan Intervention for End point reduction), which required ECG-LVH for entry, well over 2/3 of patients had abnormal diastolic function. Aggressive control of blood pressure in LIFE was associated with a near doubling of the prevalence of normal diastolic filling, over the course of the study, and a reduced risk for hospitalization for heart failure.\(^8\) Solomon et al showed in the VALI DD (Valsartan in Diastolic Dysfunction) study that aggressive treatment of hypertension, regardless of treatment strategy, was associated with improvements in diastolic dysfunction.\(^19\)

As implied earlier, we interpret these aggregate data as providing important validation of the effort made in grading diastolic function.\(^20\) More important, of course, is that we now have proof of the concept that hypertension and, possibly, hyperinsulinemia work synergistically with aging to worsen diastolic function and provide the substrate for diastolic heart failure. This body of work is proving that the more severe the diastolic dysfunction, the worse the prognosis. In popular parlance, there is a signal in this diastolic function analysis.

### Disclosures

None.

### References


Fitzgibbons and Aurigemma: Importance of Serial Changes in Diastolic Function


**Key Words:** Editorials • echocardiography • epidemiology