

EDITORIAL COMMENT

Cracking the Mysteries of Diastolic Function in Atrial Fibrillation

New Technology for an Old Problem*

Zoran B. Popović, MD, PhD, Allan L. Klein, MD

Cleveland, Ohio

Atrial fibrillation (AF) is the most common clinically significant cardiac arrhythmia with an estimated number of 2.3 million U.S. citizens affected (1). Additionally, this number will only continue to increase because of an aging U.S. population—it is estimated that the number of affected individuals will double by 2050 (1). AF is often interlinked with some cardiac dysfunction. However, assessing cardiac function, and especially diastolic function, by echocardiography in AF is difficult. For one thing, there is no atrial kick, making most frequently used algorithms for staging diastolic dysfunction not applicable (2). In addition, there is

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beat-to-beat variability. We have previously shown that although beat-to-beat variability of left ventricular relaxation shows strong nonlinear dependence on preceding cycle length variability (3), variability of left ventricular filling is influenced more by the amount of Frank-Starling mechanism activation during the preceding contraction (4). However, even after recognizing these physiological links, we are still left with the necessity of measuring multiple beats to get satisfactory approximation of average diastolic filling.

Enter the report of Kusunose et al. (5) in this issue of *JACC*. The investigators cleverly applied a new and original technology to this very old clinical problem. They used an ultrasound machine that can simultaneously record the pulsed-wave Doppler

signals of both the mitral valve inflow and mitral annular velocities. Finally, with this machine, we are provided with a tool that can circumvent the beat-to-beat variability of diastolic function seen in AF. In this report, the investigators have focused on assessing a specific marker of diastolic function—the ratio between early diastolic mitral inflow (E) velocity and early diastolic mitral annulus (E') velocity (E/E' ratio). E/E' ratio is a very well validated marker of prognosis and exercise capacity, with most of the studies performed with patients in a normal sinus rhythm (6,7). The investigators show that if the E/E' ratio is measured during a cardiac cycle in which the ratio of preceding and pre-preceding beats approaches 1 (8), it closely correlates with the E/E' ratio measured by the standard method of averaging E and E' measured from multiple nonsimultaneously acquired beats. However, more clinically important is that they also show a very good correlation with the brain natriuretic peptide level, a well-known marker of survival (9). By showing this key fact, this report confirms the clinical relevance of the E/E' ratio in difficult patients in whom diastolic function must be assessed. Additionally, the investigators also show a more modest correlation with left ventricular filling pressure.

This report provides us with 2 additional insights. The first one focuses on how little E/E' varies during AF. AF leads to wide variability of relaxation, as evidenced by beat-to-beat variability of time constant of isovolumic pressure decay (3). It is also well known that filling pressures vary widely in AF. Interestingly, despite this, the investigators have shown that the E/E' ratio varied little in their population of patients with AF. One possible explanation may be that abnormalities of relax-

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From the Cleveland Clinic Foundation, Cleveland, Ohio.

ation affect both the E-wave of the mitral inflow and the E'-wave of the mitral annulus to the same extent. Another possibility is a relatively low fluctuation in cycle length variability in this group of patients with well-controlled rate. Finally, there is a possibility that the E/E' ratio is a stable intrinsic expression of underlying cardiac abnormality that is less affected by transient changes of relaxation and filling pressures. This would be compatible with the seemingly contradictory findings that E/E' correlates very poorly with pulmonary wedge pressure in patients with severe heart failure (10), despite being an independent predictor of survival in a very similar population of patients (6).

Still, many questions remain unanswered. The subjects studied had a normal ejection fraction and relatively low pulmonary capillary wedge pressures.

Their heart rates were well controlled, with very narrow variability margins. In this setting, one could even argue that the new techniques described in this report were not necessary. It is unknown how the E/E' ratio behaves in the setting of rapid AF associated with heart failure. Also, the investigators have not examined other aspects of relationships between E and E' velocities, such as the behavior of the differences of time to onset of E versus E' (11) or the E' behavior during nonejecting beats. These issues still remain on the edge of the horizon of our current knowledge and almost certainly will be addressed by new research.

Reprint requests and correspondence: Dr. Allan L. Klein, Cleveland Clinic, 9500 Euclid Avenue, Desk J1-5, Cleveland, Ohio 44195. *E-mail:* kleina@ccf.org.

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