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EDITORIAL COMMENT

Assessing Diastology in Aortic Stenosis

Should We Stress About Strain Rate?*

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When you can measure what you are speaking about and express it in numbers, you know something about it: but when you cannot measure it . . . your knowledge is of a meager and unsatisfactory kind.
Lord Kelvin, lecture to the Institute of Civil Engineers, 1883 (1)

A method to represent diastolic function by a single measure is lacking, in part because diastole consists of distinct hemodynamic phases. Still, investigators often focus on singular aspects of diastole such as passive stiffness, active relaxation, pressure-volume relationships, or filling pressure. The hierarchical relationships among the multitude of noninvasive parameters used to assess diastolic function, therefore, is confusing at best. In this issue of *iJACC*, Dahl et al. (2) try to shed some light by analyzing the association between diastolic parameters and prognosis in patients with aortic stenosis (AS) undergoing aortic valve replacement (AVR). Specifically, the authors aimed to compare a new parameter, the early mitral inflow velocity-to-early diastolic strain rate (E/SRe) ratio, to the widely used early diastolic velocities of mitral inflow-to-mitral annulus (E/e′) ratio.

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Before discussing their results, 2 questions are worth revisiting. First, what do we know about the relationships among AS, left ventricular hypertrophy, and diastolic dysfunction? Second, which of these parameters predicts outcome after AVR? For the first question, many of the mechanistic insights come from studies conducted by Krayenbuehl and colleagues (3). In patients with AS, these studies found that chamber relaxation was impaired and that correlated with left ventricular hypertrophy (4). They also demonstrated distinct diastolic profiles according to the degree of hypertrophy. In patients with the most severe hypertrophy, early diastolic filling, chamber relaxation, and mitral valve opening pressure were all increased. In patients with less severe hypertrophy, early diastolic filling decreased but late filling increased (5).

This group also elucidated the link between myocardial structure and diastology after AVR. In patients with AS, myocardial stiffness increased early after AVR (6). That unexpected finding was explained by a relative increase in interstitial fibrosis because muscle fiber diameter decreased but fibrous content remained unchanged. Over a longer follow-up, left ventricular muscle mass continued to regress (7), and interestingly, fibrous content also decreased (3). However, muscle fiber diameter and interstitial fibrosis were still increased compared to those of controls, suggesting that these patients remain vulnerable to adverse events related to diastolic dysfunction. In fact, left ventricular hypertrophy, E/e′, and left atrial volume have all been associated with poor outcome after AVR (8–10).

In this context, Dahl et al. (2) provide further insight into the relationship between prognosis and diastolic dysfunction that occurs as a consequence of the pressure overload imposed by AS. The authors hypothesized that E/SRe would be associated with adverse outcomes after AVR and that the E/SRe ratio would provide incremental information to E/e′. The primary outcome was overall mortality, with 37 deaths over a median follow-up of 5 years. In a univariate model, age, European System for Cardiac Operative Risk Evaluation (EuroSCORE), N-terminal pro-B-type natriuretic peptide expression, left ventricular mass, left atrial volume, E/e′ ratio, global longitudinal strain, and E/SRe ratio were all associated with increased mortality. Adding left atrial volume, global longitudinal strain, or E/SRe to a baseline model that included

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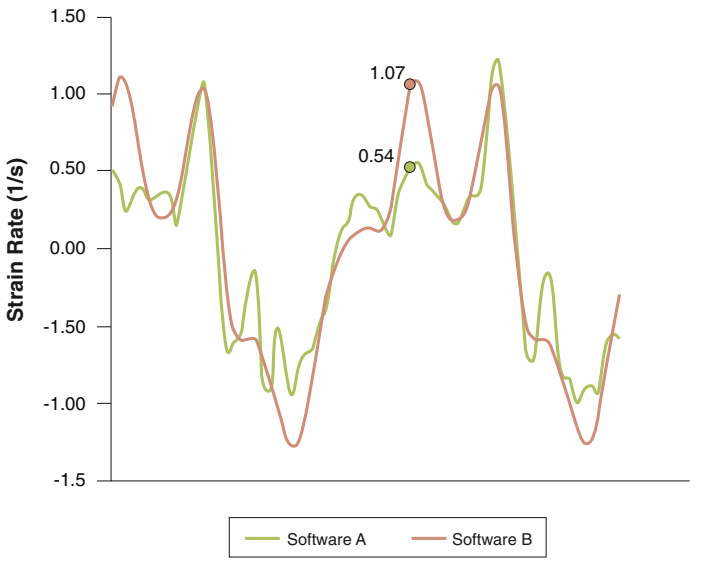
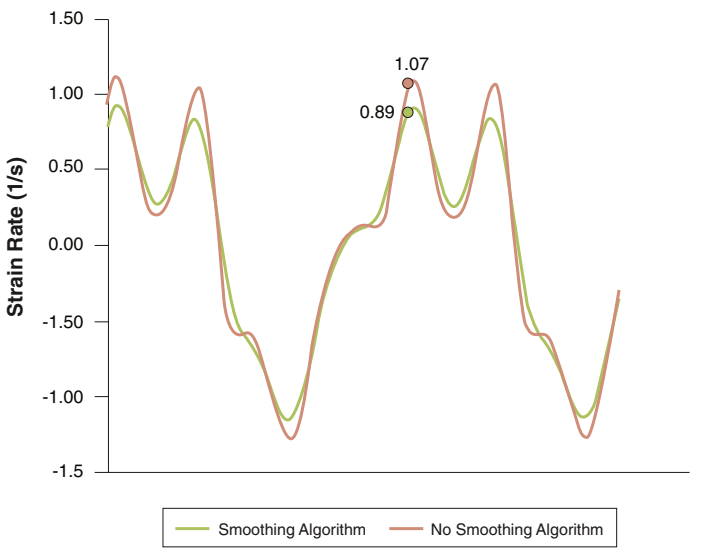
FIGURE 1 Different Software Programs and Strain Rate



Strain rate curves were obtained from the same image series representing a single cardiac cycle. There is a 2-fold difference in early diastolic strain rate values. Peak values represent peak early diastolic strain rate values.

age, diabetes mellitus, and left ventricular ejection fraction significantly improved mortality prediction. Finally, in a background model including EuroSCORE, diabetes mellitus, and left ventricular ejection fraction, E/SRe but not E/e′ significantly increased the chi-square analysis of the model. The area under the receiver operating characteristic curves for the baseline model and models including E/e′ or E/SRe were 0.67, 0.69, and 0.71, respectively.

FIGURE 2 Smoothing and Strain Rate



Smoothing decreases early diastolic strain rate by 18%. Peak values represent peak early diastolic strain rate values.

With these results, should we preferentially assess E/SRe over E/e′ in patients with AS and preserved ejection fraction? We think that this shift would be premature. Although the authors assert that the E/SRe ratio is prognostically superior to that of E/e′, they provide indirect evidence only. E/SRe significantly improved the chi-square value when added to their baseline model; however, the question is whether E/SRe improves a model that already includes E/e′. Given the correlation between the E/e′ and E/SRe ratios, it seems unlikely that such a model would significantly increase the chi-square statistical value.

However, because this was a small study with few events, the authors were conscientious to not overfit their models, and statistical issues are not of great concern. Generally, the pathophysiology seems to favor SRe over e′, but technical issues are discouraging. As recognized by professional societies, there is no consensus on what are the normal values for strain and strain rate (11). Although this may stem from software differences (**Figure 1**), problems occur even with the same software. For example, in 2 studies of strain in healthy subjects, published within 3 years of each other, the average values differed by almost ± 2 SD, a discrepancy that would label almost one-half of the subjects from 1 study as abnormal according to the criteria of the second study (12,13).

In addition, there are specific problems related to measuring strain rates. Strain rate is a high frequency signal and is sensitive to temporal filtering, performed either by the software or from too low a frame count (**Figure 2**). Finally, the simplest (and most vexing) question is, how should we report global SRe once the data are collected? The authors selected 1 of 3 possible methods. They calculated global SRe from the average of the 18 peak segmental SRe's. Upon inspection of their **Figure 1**, it is apparent that segmental SRe's are not isochronal and that their average will overestimate the SRe obtained from the nonsegmented single-view SR trace (marked by white dots [2]) in this case. SRe obtained from the average of 6 peaks was 1.24, whereas it was 1.16 when obtained from a nonsegmented single-view SR trace. A more physiological method would be to average SRe of 3 nonsegmented single-view traces or to read it directly from a single global longitudinal strain rate trace.

In conclusion, while these comments seem fastidious, they stem from our own travails with this technology and emphasize the fact that assessment of

strain and strain rate remains in an inchoate state. The work of Dahl et al. (2) is novel and encouraging, but because of these technical issues, further work and standardization are needed before SRe can be used clinically as a measurement.

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