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EDITORIAL COMMENT

Machine Learning for Electrocardiographic Diagnosis of Left Ventricular Early Diastolic Dysfunction*

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Early diastolic dysfunction is common, with a prevalence of 21% in the general adult population and 35% in patients older than 65 years of age (1,2). Although the natural history of early diastolic dysfunction is dependent on the cause, the disorder generally worsens over time (3). Early diastolic dysfunction clearly carries prognostic significance and predicts all-cause mortality (1,3). The earliest manifestation of diastolic dysfunction is impaired myocardial relaxation. This may be quantified with the time constant (τ) of the invasively measured left ventricular diastolic pressure decline curve (4). Echocardiography allows noninvasive diagnosis of early diastolic dysfunction by measuring the early filling velocity (e′) of the mitral annulus tissue Doppler trace, which correlates with τ (5).

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In this issue of the *Journal,* Sengupta et al. (6) used advanced signal processing and machine learning techniques to diagnose early diastolic dysfunction from a 12-lead electrocardiogram (ECG) in 188 patients who were referred for coronary computed tomography. The ECG signals were deconstructed in a manner similar to Fourier analysis and subsequently represented as a plot of the signal frequency versus time, which allows improved signal-to-noise ratio. A machine learning algorithm was then implemented to diagnose early diastolic dysfunction from 370 features of the processed ECG signal. These ECG signal processing and machine learning techniques demonstrated good sensitivity (80%) and specificity (84%) for diagnosing early diastolic dysfunction, and they performed even better in older, hypertensive, and obese patients. This finding is not unexpected because these patient groups are predisposed to early diastolic dysfunction (1). Wavelet transform signal processing is not novel, but as Sengupta et al. (6) point out, it has not been used for the diagnosis of early diastolic dysfunction. Truly innovative, however, is the application of a machine learning algorithm to identify relevant data points from a large number of features derived from the ECG signal. Machine learning goes beyond simple data processing and enters the realm of artificial intelligence, where computers can use logic to perform reasoning operations. This technology has been researched only on a very limited scale in cardiology, but it holds much promise for large, complex datasets ("big data") (7,8).

Early diastolic dysfunction is a recognized precursor of heart failure with preserved ejection fraction. To prevent or attenuate early diastolic dysfunction progression to heart failure with preserved ejection fraction, 3 lines of investigation will have to be pursued: 1) description of its natural history, including the time course and characteristics of patients with disease that progresses; 2) the effect of modification of risk factors and pharmacological agents; and 3) the morbidity and mortality benefits of preventing or slowing disease progression.

Researching these questions will be greatly facilitated by a cost-effective screening tool for early diastolic dysfunction. Biochemical markers of diastolic dysfunction (e.g., natriuretic peptides) have been

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used in a community setting and have demonstrated modest sensitivity (75%) and low specificity (69%) in screening for early diastolic dysfunction (9). Echocardiography alone was more cost-effective than a strategy of natriuretic peptide-directed echocardiography in detecting left ventricular dysfunction in a population at risk for heart failure, and natriuretic peptide measurement is therefore unlikely to be cost-effective for screening of lower-risk cohorts or on a population level (10). Signal-processed, machine-analyzed ECG may overcome the limitations of natriuretic peptides.

In the study by Sengupta et al. (6), the study group consisted of patients with suspected coronary artery disease who were referred for computed tomography coronary angiography. Left ventricular diastolic dysfunction is an earlier marker of significant coronary artery stenosis than is left ventricular systolic dysfunction. Patients with low e′ more frequently had significant coronary artery stenosis (>50% stenosis) as compared with patients with normal e′ (18% vs. 7.3%; $p = 0.001$), despite no differences in left ventricular ejection fraction. Signal-processed, machine-analyzed ECG could detect 82% of patients with significant coronary stenosis, and the post-test probability of stenosis increased from 55% to 64% when a low e′ was predicted. Signal-processed, machine-analyzed ECG could be a valuable tool in routine clinical practice to identify early diastolic dysfunction and coronary artery disease, 2 entities that frequently coexist.

For a signal-processed, machine-analyzed ECG diagnosis of early diastolic function to enter into clinical practice, validation will be required in larger studies, including different subgroups of patients and not only patients with suspected coronary artery disease. The importance of diagnosing early diastolic dysfunction will also be greatly enhanced when effective management strategies become available. Contemporary cardiology is focused on the use and further development of advanced imaging techniques for the diagnosis of (early) diastolic dysfunction. Sengupta et al. (6) have successfully applied advanced signal processing and machine learning to the diagnosis of early diastolic dysfunction from a standard, 12-lead surface ECG. The amount of information gleaned from an ECG in this way far surpasses any visual interpretation and expands the diagnostic potential of the 12-lead ECG. Although this approach to ECG analysis may also prove useful in cardiac disorders other than early diastolic dysfunction, machine learning has broader potential applications in cardiology and medicine. Harnessing the power of computers to aid in the interpretation of diagnostic investigations can enhance our clinical judgment as physicians, and that will benefit our patients.

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