Echocardiographic Surrogate Marker for Diabetic Cardiomyopathy

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The number of patients with diabetes mellitus (DM) continues to increase in the general population and the link between heart disease, especially diabetic cardiomyopathy, and DM is a major clinical problem. Therefore, it is important to investigate suitable surrogate markers of the early stage of diabetic cardiomyopathy in order to begin managing this disease as soon as possible. There have been several reports on echocardiographic surrogate markers for detecting diabetic cardiomyopathy because echocardiography is a simple and noninvasive technique for use in the clinical setting. One of the mechanisms of diabetic cardiomyopathy is considered to be coronary microvascular dysfunction, which may induce left ventricular (LV) dysfunction and subsequent heart failure. Determinants of microvascular dysfunction in DM, such as hyperglycemia and insulin resistance, and factors including sympathetic overdrive, endothelial dysfunction, and LV concentric remodeling, also contribute to the development of early-stage diabetic cardiomyopathy, which ultimately leads to heart failure. Therefore, we need surrogate noninvasive markers of the early stage of diabetic cardiomyopathy so that it can be managed earlier. Coronary flow reserve (CFR) is a key method for detecting microvascular dysfunction in patients with DM. Adenosine triphosphate (0.14 mg·kg⁻¹·min⁻¹) stress transthoracic echocardiography (TTE) is a reliable method for detecting diabetic cardiomyopathy, but it evaluates only the distal left ascending artery. Previously, my group reported global CFR measurements evaluated by coronary sinus flow pattern using stress transesophageal echocardiography (TEE). The CFR of the entire coronary artery system was evaluated using this TEE method, but the procedure is semi-invasive compared with TTE. In addition, stress echocardiography is not suitable as a screening test to detect early-stage diabetic cardiomyopathy because it is time-consuming and relatively complex. Therefore, markers that can be evaluated by standard echocardiography should be investigated. Several reports have identified echocardiographic markers for diastolic dysfunction, including deceleration time, the ratio of early transmitral peak velocity (E) to peak late diastolic velocity (A) using pulsed Doppler (E/A), and the ratio of E to tissue Doppler peak early diastolic velocity of mitral annulus (e’). (E/e’)^1 is useful in identifying diabetic cardiomyopathy because diastolic dysfunction is one of the mechanisms that leads to deterioration at a certain stage of diabetic cardiomyopathy. However, these echocardiographic markers for diastolic dysfunction are also correlated with LV hypertrophy or hypertension and it is usually difficult to exclude the effect of these factors from the study patients with DM.

In this issue of the Journal, Enomoto et al report that systolic function assessed by global longitudinal strain (GLS) and inner (subendocardial) circumferential strain (CS) are reduced in diabetic cardiomyopathy. GLS and inner CS were evaluated by 2-dimensional speckle-tracking echocardiography, revealing that abnormal strain is present even in normotensive patients with DM who showed neither LV hypertrophy nor diastolic dysfunction. Thus, these strain factors may be a more sensitive and specific marker for early diabetic cardiomyopathy.

Table. Echocardiographic Markers of Early Diabetic Cardiomyopathy

| Echocardiographic marker | Cardiac phase | Methodology |
|-------------------------|---------------|-------------|
| Deceleration time       | Diastolic function | TTE (pulsed Doppler) |
| E/A                     | Diastolic function | TTE (pulsed Doppler) |
| E/e’                    | Diastolic function | TTE (pulsed and tissue Doppler) |
| CFR of distal LAD       | Diastolic>systolic function | Stress TTE (pulsed Doppler) |
| CFR of coronary sinus   | Diastolic>systolic function | Stress TEE (pulsed Doppler) |
| GLS                     | Systolic function | TTE (speckle-tracking strain imaging) |
| Inner GCS               | Systolic function | TTE (speckle-tracking strain imaging) |

A, transmitral peak late diastolic velocity; CFR, coronary flow reserve; E, transmitral peak early diastolic velocity; e’, peak early diastolic velocity of mitral annulus; GCS, global circumferential strain; GLS, global longitudinal strain; LAD, left anterior descending artery; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.
sensitive marker for diabetic cardiomyopathy than diastolic dysfunction markers, even though these strain markers could not be obtained in approximately 10% of patients because of poor echocardiographic images, and strain factors, especially inner CS, could not be measured by all standard echocardiographic machines. More recently, it was reported that GLS may not be impaired in type 1 DM. That is, the deterioration involved in diabetic cardiomyopathy may be attributable to different mechanisms in types 1 and 2 DM. To confirm the correlation between GLS and diabetic cardiomyopathy, a large-scale randomized clinical trial of DM patients must be conducted.

The progression of heart failure caused by diabetic cardiomyopathy is correlated with many risk factors, including hyperglycemia, insulin resistance, sympathetic overdrive, endothelial dysfunction and LV concentric remodeling from hypertension. Enomoto et al also report that GLS is correlated with obesity and blood pressure even in normotensive patients with DM.

To prevent heart failure caused by diabetic cardiomyopathy, high-risk patients with diabetic cardiomyopathy should be identified using echocardiographic surrogate markers, including strain factors, so that these patients can receive instruction on the early reduction of risk factors such as obesity and hypertension.

Disclosures

I have no conflicts of interest to declare.

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