

## Assessing Contractile Function When Ejection Fraction Is Normal A Case for Strain Imaging

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Two-dimensional (2D) speckle-tracking echocardiography has, in recent years, emerged as a new method for assessing left ventricular systolic and diastolic function.<sup>1</sup> The technique measures the movement of nonrandom coherent speckles in 2D echocardiographic images. Speckle-tracking measures myocardial deformation through the heart cycle rather than volumetric changes between end-diastole and end-systole, the standard method for calculating left ventricular ejection fraction (LVEF), which is dependent on image quality, the ability to accurately trace the endocardial border, and geometric assumptions required to estimate volumes from a 2D image.<sup>2</sup>

### See Article by Palmieri et al

Assessment of global longitudinal strain (GLS), obtained by 2D speckle-tracking echocardiography, requires the presence of sufficient amount of speckles within the myocardial wall for tracking to work and is now present as a semiautomatic function in many ultrasound machines and in off-line devices. Two-dimensional speckle-tracking echocardiography has been shown to be a promising technique, and GLS provides an objective measurement of cardiac function, which has been demonstrated to be of prognostic value in the general population<sup>3</sup> and in patients having a wide array of cardiac diseases, including patients with a myocardial infarction<sup>4</sup> and patients with heart failure (HF) with reduced<sup>5</sup> and preserved LVEF.<sup>6</sup> Furthermore, myocardial deformation imaging has allowed for increasing recognition of subtle abnormalities of the LV function with a preserved LVEF. LV deformation is altered despite preserved LVEF in conditions predisposing to HF, including increasing age,<sup>7</sup> hypertension,<sup>8</sup> diabetes mellitus,<sup>9</sup> stable angina,<sup>10</sup> renal dysfunction,<sup>11</sup> and obesity.<sup>12</sup> Likewise, in patients with prevalent HF with preserved LVEF, longitudinal strain is impaired,<sup>13</sup> despite a relative normal LVEF. These conditions are accompanied by a distinct pattern

of deformation characterized by impaired longitudinal strain and exaggerated circumferential strain.<sup>14</sup>

Recent studies have demonstrated that a impaired myocardial deformation, as assessed by low GLS, seems to provide incremental prognostic information to LVEF about the risk of cardiovascular morbidity and mortality, especially when LVEF is relatively preserved.<sup>3,4,6</sup> Similar results are presented in the current issue of *Circulation: Cardiovascular Imaging*, where Palmieri et al<sup>15</sup> report an interesting article, which aims to investigate whether GLS provide incremental prognostic information in patients admitted to a subintensive medical unit with severe sepsis or septic shock.<sup>15</sup> This prospective study included 115 patients admitted to a single subintensive medical unit, who had an echocardiogram performed within 24 hours of admission. Follow-up on mortality was assessed at 7 and 28 days after admission. The authors found that GLS was an independent predictor of all-cause mortality after 7 days of follow-up and borderline predictive at 28 days of follow-up. In comparison, LVEF was not predictive of mortality at neither 7 nor 28 days of follow-up. In addition, the authors found that GLS particularly improved risk stratification in patients with a preserved LVEF (defined as LVEF>30%). In patients with low LVEF, both GLS and LVEF were capable in identifying patients in high risk of mortality, but in the high LVEF spectra, fatal events were distributed across a wide range of LVEFs, whereas almost all deceased patients had GLS<15%, despite relatively preserved LVEF.<sup>15</sup> Besides being the largest prospective study assessing the usefulness of GLS to predict outcome in patients with sepsis, the authors also display, like other reports have done previously,<sup>3,4,6</sup> that GLS especially seems to provide incremental information about outcomes in the setting of a preserved LV systolic function as assessed by LVEF. Therefore, when LVEF is low, all cardiologist are well aware that the patient is at high risk, however, when LVEF is preserved, we need additional and other information about cardiac function, and GLS might be the clinical tool to use. However, the mechanism by which these fairly subtle abnormalities of LV systolic function, as assessed by low GLS, may predispose to adverse outcomes is unclear.

The answer might be found in the anatomic distribution of myocardial fiber orientation of the heart and the difference in methodology between 2D speckle-tracking echocardiography and volumetric methods. The LV myocardium consists of myocardial fibers with differing orientations. The cardiac midwall is occupied by circumferential fibers, whereas longitudinal fibers form a right-handed helix in the subendocardium and a left-handed helix in subepicardium.<sup>16</sup> Therefore, the subendocardial and subepicardial fibers represent 2 oppositely directed spirals, with the net difference in myofiber angulation

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between these 2 spirals ranging from  $+60^\circ$  to  $-60^\circ$ .<sup>17</sup> Although both the subendocardial and the subepicardial longitudinal fibers contribute to longitudinal deformation, in the normal heart, they counterbalance each other's ability to produce circumferential deformation. The subendocardial fibers seem more susceptible to dysfunction<sup>10,18</sup> than the mid and epicardial fibers. This impairment of the subendocardial longitudinal fibers also leads to attenuated subendocardial right-handed helix fiber shortening during systole, potentially resulting in a failure to fully counterbalance the subepicardial left-handed helix fiber shortening and resulting in increased circumferential deformation.<sup>4,13,19</sup> This putative mechanism for early alterations in LV deformation is consistent with the previously reported results that GLS is impaired despite preserved LVEF in various populations, including increasing age,<sup>7</sup> hypertension,<sup>8</sup> diabetes mellitus,<sup>9</sup> stable angina,<sup>10</sup> renal dysfunction,<sup>11</sup> obesity,<sup>12</sup> and HF with preserved LVEF.<sup>13</sup> Indeed, this increased circumferential deformation, which accompanies a reduced longitudinal deformation, merely because of the anatomic fiber direction within the cardiac wall, might be one of the major determinants of why LVEF remains within the normal range despite an ailing heart. In addition, this mechanism, therefore, also explains why subclinical impaired longitudinal deformation seems to provide prognostic information beyond LVEF in the setting of preserved LVEF conditions.

Yet another reason for longitudinal myocardial deformation to be especially useful in the setting of a preserved LVEF might simply be because of the difference in methodology. As previously mentioned, the assessment of LVEF is based on the percentage difference in volume between end-diastole and end-systole, whereas GLS is a measure of the percentage the LV myocardial walls shortens in length during the cardiac cycle.<sup>1</sup> Furthermore, cardiac function has traditionally been divided into systolic and diastolic function, where LVEF is the echocardiographic measure of systolic function, while several flow and tissue Doppler measures, in conjunction with the left atrium size, defines echocardiographic determined diastolic function. However, these theoretically determined definitions on cardiac function seem less relevant when assessing cardiac function using LV longitudinal deformation. Several diseases, which formerly were considered as associated with isolated impaired diastolic function, such as hypertension and hypertrophy, are now recognized to display impaired longitudinal deformation with preserved LVEF.<sup>6,8,13</sup> During systolic contraction, the ventricular cardiomyocytes shorten to less than their equilibrium length, which stores potential energy in the elastic myocardial components (the extracellular collagen surrounding the myocytes and the titin filaments within the myocytes). This accelerates the relaxation process, contributes to relengthening during early diastole, and aids filling by moving the mitral annulus around the column of the incoming blood.<sup>16,20</sup> Systolic function as determined by longitudinal deformation is therefore indeed a determinant of the diastolic function and vice versa.<sup>21</sup> LV longitudinal deformation might therefore identify subtle impairments in cardiac function, which previously was recognized as being isolated diastolic dysfunction in the setting of preserved LVEF, and these impairments have been demonstrated to be strong prognosticators.<sup>3,4,6</sup>

Palmieri et al<sup>15</sup> add yet another clinical disease to the continued expanding list of diseases, where assessing LV longitudinal deformation might improve risk stratification. In addition, the authors also add to the increasing evidence demonstrating that LV longitudinal deformation identifies subtle cardiac dysfunction, regardless of LVEF, which provides prognostic information above and beyond what we can obtain from our conventional echocardiographic measures, and further supports the argument that it may be time to move beyond LVEF in assessment of cardiac function.<sup>2</sup>

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## Disclosures

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