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Geometry as a Confounder When Assessing Ventricular Systolic Function

Comparison Between Ejection Fraction and Strain

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ABSTRACT

BACKGROUND Preserved left ventricular (LV) ejection fraction (EF) and reduced myocardial strain are reported in patients with hypertrophic cardiomyopathy, ischemic heart disease, diabetes mellitus, and more.

OBJECTIVES The authors performed a combined mathematical and echocardiographic study to understand the inconsistencies between EF and strains.

METHODS An analytical equation showing the relationship between EF and the 4 parameters, global longitudinal strain (GLS), global circumferential strain (GCS), wall thickness, and short-axis diameter, was derived from an elliptical LV model. The equation was validated by measuring the 4 parameters by echocardiography in 100 subjects with EF ranging from 16% to 72% and comparing model-predicted EF with measured EF. The effect of the different parameters on EF was explored in the model and compared with findings in the patients.

RESULTS Calculated EF had very good agreement with measured EF ($r = 0.95$). The model showed that GCS contributes more than twice as much to EF than GLS. A significant reduction of GLS could be compensated by a small increase of GCS or wall thickness or reduced diameter. The model further demonstrated how EF can be maintained in ventricles with increased wall thickness or reduced diameter, despite reductions in both longitudinal and circumferential shortening. This was consistent with similar EF in 20 control subjects and 20 hypertrophic cardiomyopathy patients with increased wall thickness and reductions in both circumferential and longitudinal shortening (all $p < 0.01$).

CONCLUSIONS Reduced deformation despite preserved EF can be explained through geometric factors. Due to geometric confounders, strain better reflects systolic function in patients with preserved EF. (J Am Coll Cardiol 2017;70:942-54)

Numerous studies have reported a significant reduction in left ventricular (LV) global longitudinal strain (GLS) without a corresponding reduction of LV ejection fraction (EF) in various study populations, including patients with heart failure with preserved EF, coronary artery disease (CAD), diabetes mellitus, hypertensive heart disease, hypertrophic cardiomyopathy (HCM), and electrical disease (1-6).

The majority of longitudinally-oriented fibers are located in the subendocardium, which is considered most susceptible to myocardial disease, including

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ischemia. Many studies have shown that GLS detects subtle longitudinal abnormalities that do not affect EF globally (7). It remains uncertain, however, whether a small loss of longitudinal function per se is negligible for global pump function or if compensatory effects by other determinants of EF are responsible for preserving EF. A common hypothesis is that circumferential fibers in the midwall, if intact, may compensate for the loss of longitudinal mechanics to preserve LV pump function and EF (7,8). However, several studies report a significant reduction in both GLS and global circumferential strain (GCS), despite normal LVEF (1,9,10). The mechanism maintaining EF in this setting is unclear. MacIver (11,12) has proposed a geometric explanation for this apparent paradox: using a computational model of a truncated ellipsoid, he showed that increased wall thickness could effectively preserve EF. However, the computational model was not validated, and the effect of other geometric factors on EF remains incompletely described.

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The general objective was, therefore, to perform a comprehensive study of the individual geometric factors that influence EF by combining clinical data from speckle tracking echocardiography and mathematical modeling.

Two specific objectives of this study were to investigate if:

1. The contribution of longitudinal shortening to EF is so small that reduced longitudinal shortening can be compensated by small changes in other factors to preserve EF; and
2. EF can be preserved, despite reductions in both longitudinal and circumferential shortening in LVs with increased wall thickness and/or reduced end-diastolic volume (EDV).

METHODS

PATIENT STUDY. Echocardiographic examinations from 100 subjects were retrospectively included. The study population was heterogeneous to represent a wide range of EF values: 20 patients had significant CAD; 20 patients had angina pectoris without significant CAD; 20 patients had dilated cardiomyopathy (DCM); 20 patients had HCM; and 20 subjects were healthy individuals (Table 1). The inclusion criteria were adequate image quality in 3 apical views (4-chamber, 2-chamber, and long-axis) and at least 2 parasternal short-axis views (mitral valve, midventricle, and/or apical levels). Patients with exclusion of more than 6 of 18 strain segments in either apical or parasternal views were excluded. Written informed consent was obtained from all subjects.

ECHOCARDIOGRAPHY. Two-dimensional grayscale echocardiography was performed with Vivid 7 or E9 scanners (GE Vingmed Ultrasound, Horten, Norway). The frame rate was >50/s. Images were analyzed using EchoPAC version 112 (GE Vingmed Ultrasound). LV diameter and wall thickness were obtained by M-mode measurements or 2-dimensional mode. LVEF was calculated by 1 operator (SIS) using the modified Simpson's rule based on 4- and 2-chamber images (13).

Myocardial strain was measured by another operator (TMS), blinded to EF calculations, using 2-dimensional speckle-tracking echocardiography in accordance with current recommendations (14). The endocardial border was traced at end-systole, and the thickness of the region of interest (ROI) was adjusted to include most of the myocardium, but avoiding stationary speckles close to the pericardium. Longitudinal strain was measured in the 3 apical views, and circumferential strain was measured in the 3 short-axis views. All segmental strain values were measured from the same frame in end-systole, defined by the aortic valve closure in apical long-axis view. Strains were assessed at end-systole, as this is the time when minimum volume is assessed and there is a direct geometric link between EF and strains. Strain values from the 18 LV segments were averaged to GLS and GCS.

LV MODEL. We modeled the LV as a thick-walled, truncated ellipsoid (Figure 1A) (15), and derived the analytical mathematical relation for EF as a function of GLS, GCS, end-diastolic (ED) LV wall thickness (w), and ED short-axis diameter (d), as shown in Equation 1 (Online Appendix 1 shows how the equation was derived):

$$EF = \left(1 - \frac{\left(\frac{GCS}{100\%}+1\right)^2 \cdot \left(\frac{GLS}{100\%}+1\right) \cdot \left(\frac{d}{2}+f\cdot w\right)^2 - 2\cdot c\cdot f\cdot w\cdot\left(\frac{d}{2}+f\cdot w\right) + c\cdot f^2\cdot w^2}{\left(\frac{d}{2}\right)^2}\right)\cdot 100\% \quad \text{(Equation 1)}$$

The speckle tracking ROI is placed manually, and its center may not be exactly at the midwall. In the model, we therefore included a factor (f) with value between

ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease
DCM = dilated cardiomyopathy
ED = end-diastole/diastolic
EDV = end-diastolic volume
EF = ejection fraction
GCS = global circumferential strain
GLS = global longitudinal strain
HCM = hypertrophic cardiomyopathy
LV = left ventricle/ventricular
ROI = region of interest