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Role of Mathematical Modelling for Cardiac Function Evaluation in Heart Failure Patients

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Abstract
The development of patient-specific (PS) cardiac models is increasing exponentially in order to reach highly detailed description of anatomy and mechanical simulation of the organ. This is growing in parallel with computational tools, becoming day-by-day more and more sophisticated.
This study stands at this projection of large-scale performance of cardiac models and chases the challenge to find the right substitute for CT and MRI imaging techniques to make the modeling process easier to develop without loss of patient-specific feature.
It is important to focus on using ECHO images as the source for anatomical 2D geometry for patient affected by heart failure. There are many issues in understanding a priori if the patient can benefit from CRT implantation and Echocardiography is one of the first and most common test to which the patient has to undergo in this field.
An echo image-based computational model uses data from a routine test, first used for cardiac pathological patients for quantification and assessment of the disease, looking forward for hospital resource savings.

Introduction
Recent advances in medical imaging, mathematical modelling tools, and computational infrastructure have enabled estimations of in vivo tissue properties and regional mechanical function (e.g., stress and strain) using measurements of ventricular geometry, wall deformation, and loading conditions.
Research related to subject-specific estimation of the mechanical function of tissue in vivo has attracted great interest in the clinical community because it has the potential to allow for more effective stratification of different types of HF, provide insight into

the causes of HF on a subject-specific basis, and inform the design of mechanism-targeted treatments[1].

Mathematical modeling is being increasingly recognized within the biomedical sciences as an important tool that can aid the understanding of biological systems. Mathematical models of cardiovascular physiology have developed in the last century thanks to fundamental experimental work in physiology and theoretical developments in mathematics and other sciences. Patient-specific mechanical models of the whole heart for optimization and advancement of therapy represent some of the most sophisticated models developed to date[2].

Noninvasive assessment of regional myocardial function is important to the field of cardiovascular medicine to diagnose disease, assess therapeutic interventions, and predict clinical outcomes. Although magnetic resonance imaging and computed tomography imaging are useful diagnostic alternatives, echocardiography remains advantageous for widespread clinical use because of its portability, low risk, and comparatively high temporal resolution[3].

The assessment of left ventricular (LV) function is an essential component in the evaluation of any patient with heart disease. Echocardiography is now a well-established widely used, noninvasive technique to evaluate the status of the LV with clinical and prognostic significance.

The initial echocardiographic technique for evaluating LV function utilized M-mode echocardiography (MME). However, because of the small portion of the heart examined by the narrow M-mode beam and because of uncertainty of spatial orientation with MME, the noninvasive assessment of LV ejection fraction (EF) is moving toward the two-dimensional echocardiogram (2DE), using assumptions about the geometry of the LV and applying appropriate mathematical formula. However, this technique using state-of-the-art computing is time consuming and limited by factors restricting image quality, especially chronic obstructive pulmonary disease and obesity, which are not uncommon among patients with coronary artery disease[4].

Echocardiographic strain imaging, also known as deformation imaging, is a technological advancement that has been developed as a means to objectively quantify regional myocardial function. First introduced as a post-processing feature of tissue Doppler imaging (TDI) with velocity data converted to strain and strain rate, strain imaging information has more recently also been derived from speckle tracking computer processing[3].

Cardiac resynchronization therapy (CRT) has been demonstrated to be beneficial in patients with end-stage heart failure despite optimized medical therapy. Various studies have shown improvement in heart failure symptoms, exercise capacity and left ventricular (LV) systolic function [5]. However, patient responses to CRT vary significantly.

Methods

Mathematical Modelling of the Left Ventricle

Current methods for modelling left ventricular contraction are complex and so difficult to employ. Therefore, there is a need for a simpler mathematical method. To remove both confounding factors and the effects of any confusing or opposing physiological responses a mathematical model has been developed and recently published. The model has been extended to assess the effect of ventricular remodelling following normalisation stroke volume to mimic the chronic phase of heart failure.

Basic Model

The method employs one or other of two well-established three-dimensional internal (*I*) left ventricular geometric shapes using a combination of the area perpendicular to the long-axis at the level of the mitral valve and length (L) of long-axis to determine internal left ventricular volume (see Figure 1).

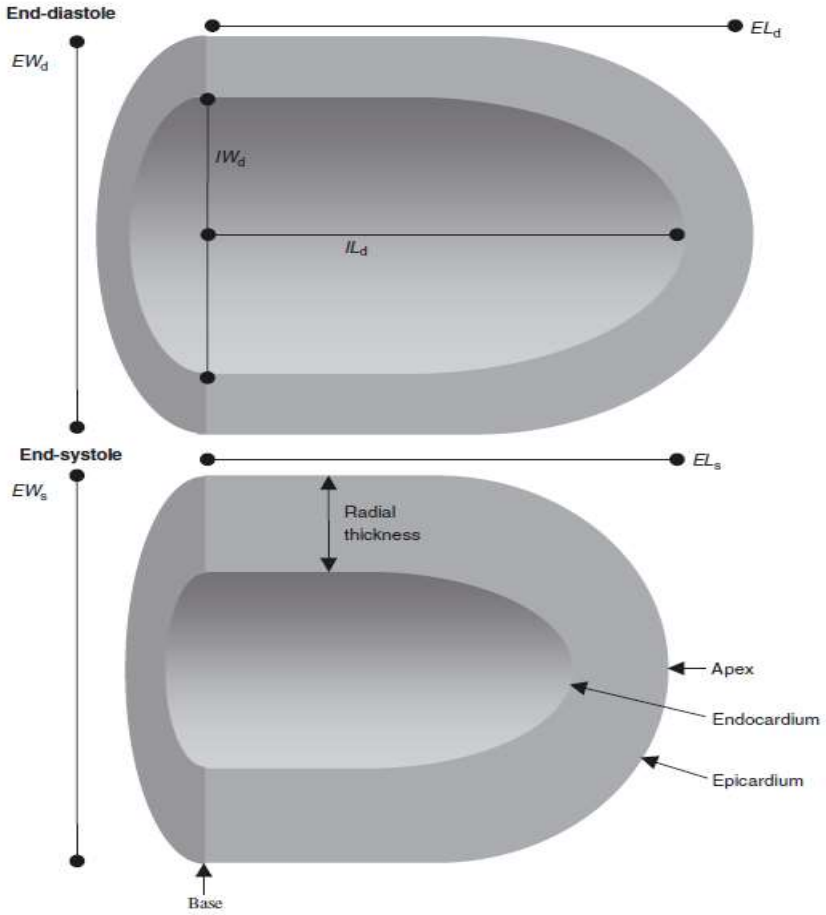

Figure 1 Schematic diagram of the left ventricle used in the model to calculate internal (*I*) and external (E) volumes during diastole from the short-axis diameter/width (IW_d & EW_d)and long-axis length (IL_d & EL_d) [6].

If one assumes that the external (E) left ventricular volume is a similar shape to the internal volume then total or external left ventricular volume can be calculated using the same formula. The apex, base, endocardium and epicardium are labelled. The diastolic external and internal volumes are calculated and the myocardial volume obtained from the difference. The external short-axis width and length are reduced to simulate systole (EW_s & EL_s, respectively) and the new external volume calculated. The internal end-systolic volume is calculated by subtracting the muscle volume from the external end-systolic volume [6]**.**

The total myocardial volume is derived from the difference in total (external) left ventricular volume and the internal volume (Figure 1). Two different formulae are available and each assumes a slightly different geometry of the left ventricle:

(a) Area-length method of Dodge

$$V = \frac{\pi}{6} W^2 . L \qquad \text{..... (1)}$$

where V = volume, W =width (i.e. short-axis diameter), L =long-axis length.

So External volume in diastole $= \frac{\pi}{6} {EW_d}^2 . EL_d$ ..... (2)

Internal volume $= \frac{\pi}{6} {IW_d}^2 . IL_d$ ..... (3)

where I =internal, E = external, d=diastole

Myocardial volume = External volume _ Internal volume ..... (4)

(b) Hemi-cylinder-hemi-ellipsoidal method

$$V = \frac{5\pi}{6} . \frac{W^2}{2} . L \qquad \text{.... (5)}$$

Major and Minor Axis and Wall Thickness [7]

The major axis (L) is determined during data acquisition as the longest distance within the contour, given that the origin must coincide with the first indicated contour point (usually the junction of the mitral and aortic valve). This is implemented by a simple search procedure. The effective minor axis is then given by

$$M = \frac{4A}{\pi L} \qquad \text{.... (6)}$$

and ventricular volume (V) is estimated by

$$\text{V} = \frac{\pi}{6} LM^2 \qquad \text{..... (7)}$$

When a wall thickness is available, the ventricular wall volume is calculated as

$$WV = \frac{\pi}{6} [(L + 2h)(M + 2h)^2 - LM^2] \qquad \text{.....(8)}$$

Stress

Given the actual three-dimensional geometry and transmural pressure, it is possible in theory to determine wall stress in all directions and as a function of position.
In general, this is a hopelessly complex computational task and a number of conventions have been established to make stress determination both easier and more meaningful. Basically, the heart is viewed as a thick-walled ellipse of revolution. Stress is calculated in the mid-wall at the equator in the circumferential direction.

$$\sigma = \frac{P(M+h)}{2h}\left[1 - \frac{(M+h)^3}{2L^2(M+2h)}\right] \quad \text{..... (9)}$$

If M and L are set equal and h is small compared to M, then this approaches La Place's-law

$$\sigma = \frac{PM}{4h} \quad \text{..... (10)}$$

Stress and pressure have the same units and are directly comparable. Physiologically, such a comparison is a measure of the mechanical efficiency of the heart geometry (eccentricity and ratio of radius to wall thickness). That is, this efficiency represents the ability of the heart to develop pressure from the contraction of the muscle tissue. Alternatively, this efficiency can be viewed as the demand placed on the muscle by the bodies requirements to maintain pressure.
The peak in stress occurs early in ejection and then falls even while LV pressure is increasing, representing an increasingly efficient geometry as the heart contracts. La Place's law shows that stress is proportional to the minor axis (M) and inversely proportional to wall thickness (h). As M decreases and h increases during ejection, the geometric factors argue for a diminution in wall stress as the heart contracts. During heart failure a dilated heart may require even greater wall stress than normal and yet generate diminished LV pressure [8].

EF, End-Diastolic Volume (EDV) and End-Systolic Volume (ESV) Algorithms

Modified Simpson's Rule

The left ventricle was considered the sum of a cylinder (from the base of the heart to the mitral valve), a truncated cone (from the level of the mitral valve to the level of the papillary muscles), and below this another cone to the cardiac apex. These three sections were arbitrarily assumed to be of equal height (L/3). The paucity of reproducible landmarks precluded the use of more than three sections (as would ideally be the case in a true Simpson's rule application) [9].

An ellipsoid model using biplane data

Two perpendicular echo planes (the mitral valve and apical view) were substituted for two angiographic projections. The apical (horizontal in figure 2.11) plane minor

(septal-posterolateral) axis is derived from the image area (A1) and its longest length (L). For this model the mitral plane is arbitrarily assumed to be midway between the base and apex. The mitral (vertical in figure 2) plane minor axis is derived from the area (Am) and the septal-posterolateral dimension (D) of the mitral level image [10].

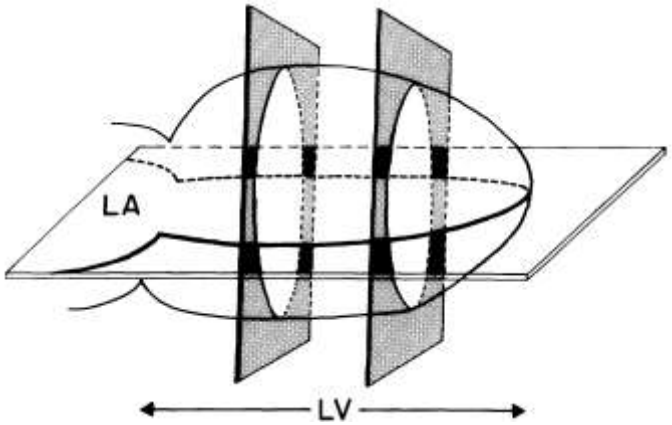

Figure 2 Schematic diagram of the left atrium (LA) and left ventricle (LV), with stippled planes indicating the projection of two-dimensional images [10].

An ellipsoid Model Using Single-Plane Data

Area (A1) and length (L) from the apical echocardiographic image were substituted into the standard single-plane area-length equation [11].

A Hemisphere-Cylinder Model Using Biplane Data

The cross-sectional area (Am) at the mitral valve level and long axis (L) from the apical view were used to solve for volume of a cylinder capped on one end by a hemisphere with a base area (Am) and height (L/2) equal to that of the cylinder [12].

A Modified Ellipsoid Model Using Unidimensional Data

The septal-posterior wall dimension (D) was substituted into a formula described by Teichholz based upon an ellipsoid model where the major axis

$$2\left(\frac{7}{2.4+D}\right)D \qquad \text{…….. (11)}$$

D is a variable function derived from the measured minor axis. This formula is intended to compensate for the deviation from the ellipsoid model seen in both unusually large and small ventricles [12].

Left Ventricular Strain

Myocardial regional mechanics assessed by echocardiographic approaches have been described by 4 principal types of strain or deformation: longitudinal, radial, circumferential, and rotational (Fig. 3). Although myocardial fiber orientation results in these strain vectors occurring 3 dimensionally in an integrated manner, most investigative works have been done using individual strain assessments. The term *strain* applied to echocardiography in a simplistic sense is to describe lengthening, shortening, or thickening, also known as regional deformation.

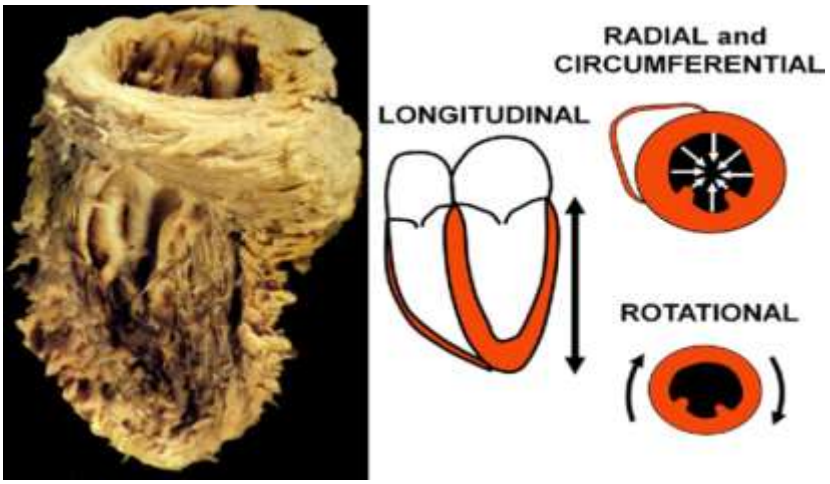

Figure (3) Myocardial Fiber Orientation and Principal Vectors of Left Ventricular Strain [13].

Strain may be $\varepsilon = \Delta L/L_o$ understood as an example of an infinitesimally thin bar where the only possible deformation is lengthening or shortening. Accordingly, linear strain or the amount of deformation can be defined by the change in length divided by the original length expressed by the formula: $\varepsilon = \Delta L/L_o$, where ε= strain, ΔL = change in length, and L_o= original length. In reality, the myocardial wall as a 3-dimensional (3D) object has strain that may occur along 3 planes (x-, y-, and z-axes), known as normal strains, and 6 shear strains [14].

Despite the complexities of myocardial wall dynamics, some meaningful information has been derived using the simplified linear strain or deformation model by echocardiography [13].

The first description of echocardiographic strain was derived from TDI velocity data using the Doppler equation to convert ultrasound frequency shifts to velocity information along the scan lines. Because the fundamental data produced by TDI were velocity information, strain rate (strain per unit of time) was derived from the velocity data using the equation:

$$\varepsilon = \frac{V_1 - V_2}{L} \qquad \ldots\ldots (12)$$

where ε= strain rate, V_1velocity at point 1, V_2velocity at point 2, and L =length, usually set at 10 mm. Strain rate and strain data using TDI required the direction of the myocardial wall motion to be along the ultrasound scan line. Longitudinal shortening using the apical windows was often used because of the favorable Doppler angle of incidence (Fig. 4) , dashed line indicates orientation of ultrasound beam. Distance along beam is denoted r. Strain rate is calculated by subtracting v (r+Δr) from v (r) over distance Δr between these 2 points. When velocities are equal, strain rate is zero and there is no compression or expansion. If v (r+Δr)> v(r), strain rate is negative and there is compression. When v (r) exceeds v (r+Δr), strain rate is positive, indicating expansion [14].

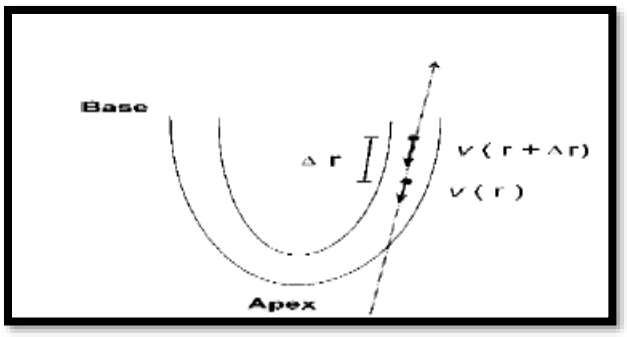

Figure 4 Schematic of how strain rate of tissue segment (Δr) is estimated from tissue velocity (v) [14].

The alternative was from the parasternal views where the relative transmural change in velocity could be calculated as the velocity gradient, similar to strain rate (e.g., in the posterior wall) [15]. TDI strain rate data could be integrated over time to determine strain (Fig. 5). Because all TDI information is affected by the Doppler angle of incidence, Doppler angle correction analysis programs were developed to determine wall motion for regions where the motion was not aligned with the Doppler scan line [16]. However, it remained impossible to assess wall motion by TDI when the angle of motion was close to 90°. Accordingly, the majority of the published literature on echocardiographic strain imaging using TDI assessed longitudinal strain from the apical windows with left ventricular (LV) shortening and lengthening aligned with the Doppler scan lines.[13]

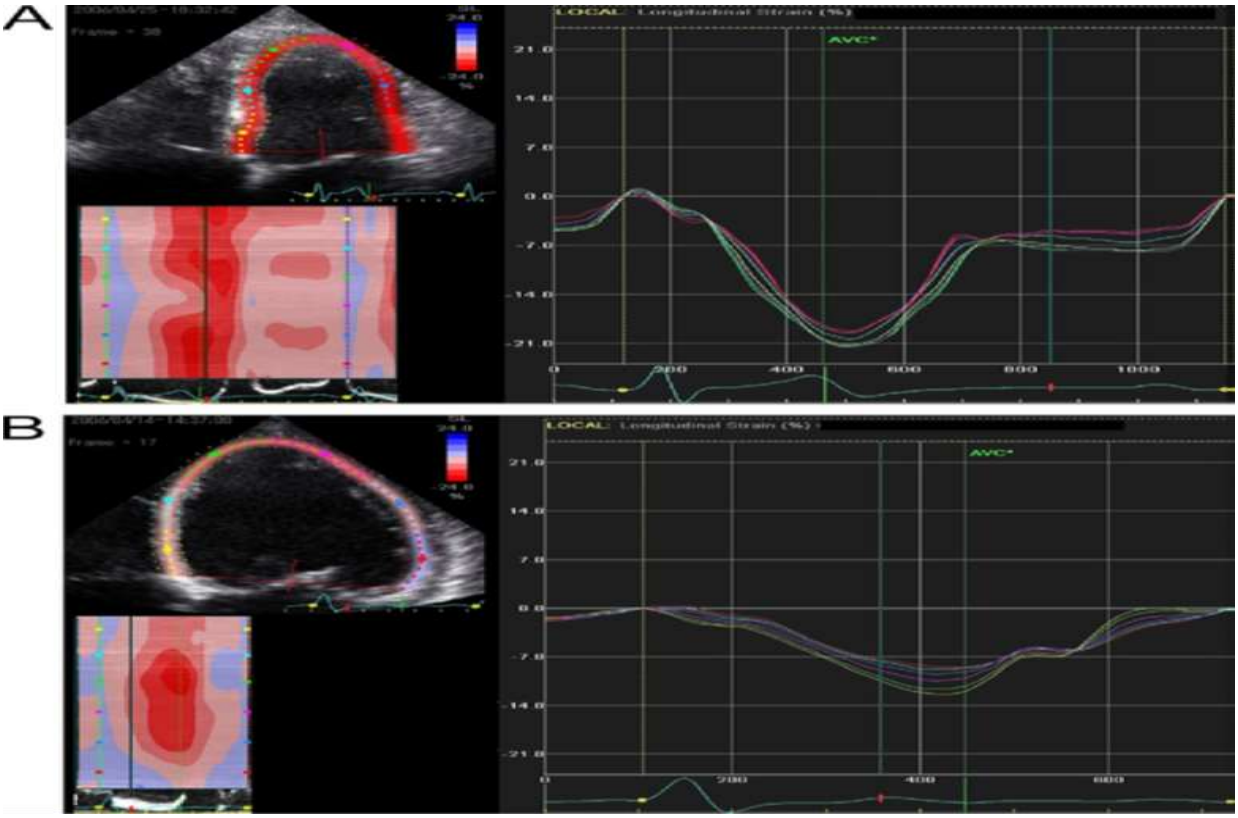

Figure (5) Longitudinal Strain by Speckle Tracking Imaging in a Normal Subject and a Heart Failure Patient (A) An example of speckle tracking imaging of longitudinal strain using the apical 4-chamber view in a normal subject. (B) An example of speckle tracking imaging of longitudinal strain using the apical 4-chamber view in a heart failure patient [15].

Conclusion

Current methods for modelling left ventricular mechanics are complex and so difficult to employ. Therefore, there is a need for a simpler mathematical method. To remove both confounding factors and the effects of any confusing or opposing physiological responses a mathematical model has been developed and recently published. The model has been extended to assess the effect of ventricular remodelling following normalisation stroke volume to mimic the chronic phase of heart failure.

Looking at a future projection of PS models in clinical and daily routine, the complex and labor-intensive process of generating models might be in contrast with surgery and diagnostic world where relatively fast turnaround times are required. This consideration leads to think a possible way clinician might have to build a time-realistic PS anatomical and mechanical model with fast, low-cost technique with the aim to study the best customized treatment without wasting of time and resources.

This task must face the compromise between highly detailed-accurate-expensive modeling on one side and a modeling based on easy method of calculation, low-cost, relative-fast, non-invasive test on the other side.

The model has allowed the facility to determine the cardiac mechanics by measuring the degree of left ventricular hypertrophy on ejection fraction, stroke volume, wall stress and strain by using left ventricle images obtained from 2D echocardiography. Also, it allows the assessment of changes in shape, size and shortening of the left ventricle which is important to predict the effect of CRT device in heart failure patient.

References

1. Wang VY, Nielsen PMF, Nash MP (2015) Image-Based Predictive Modeling of Heart Mechanics. Annu Rev Biomed Eng 17:351–383. https://doi.org/10.1146/annurev-bioeng-071114-040609

2. Trayanova NA (2011) Whole-heart modeling : Applications to cardiac electrophysiology and electromechanics. Circ Res 108:113–128. https://doi.org/10.1161/CIRCRESAHA.110.223610

3. MacIver DH (2012) The relative impact of circumferential and longitudinal shortening on left ventricular ejection fraction and stroke volume. Exp Clin Cardiol 17:5–11

4. Mueller X, Stauffer JC, Jaussi A, et al (1991) Subjective visual echocardiographic estimate of left ventricular ejection fraction as an alternative to conventional echocardiographic methods: Comparison with contrast angiography. Clin Cardiol 14:898–902. https://doi.org/10.1002/clc.4960141108

5. Inparys F, Universitaire CH, Hospital H, et al (2001) Biventricular Pacing Patients with Heart Failure and and Interventricular Conditionelay Effects of Multisite Biventricular Pacing in Patients With Heart Failure and Intraventricular Conduction. N Engl J Med 344:873–880

6. MacIver DH (2008) A mathematical model of left ventricular contraction and its application in heart disease. 35:65–86. https://doi.org/10.2495/978-1-84564-096-5/04

7. Brower RW, Meester GT, Hugenholtz PG (1975) Quantification of Ventricular Performance: A Computer-Based System for the Analysis of Angiographic Data. Cathet Cardiovasc Diagn 1:133–155. https://doi.org/10.1002/ccd.1810010204

8. McHale PA, Greenfield JC (1973) Evaluation of several geometric models for estimation of left ventricular circumferential wall stress. Circ Res 33:303–312. https://doi.org/10.1161/01.RES.33.3.303

9. Folland ED, Parisi AF, Moynihan PF, et al (1979) Assessment of left ventricular ejection fraction and volumes by real-time, two-dimensional echocardiography. A comparison of cineangiographic and radionuclide techniques. Circulation 60:760–766. https://doi.org/10.1161/01.CIR.60.4.760

10. Dodge HT, Sandler H, Ballew DW, Lord JD (1960) The use of biplane angiocardiography for the measurement of left ventricular volume in man. Am Heart J 60:762–776. https://doi.org/10.1016/0002-8703(60)90359-8

11. Kennedy JW, Trenholme SE, Kasser IS (1970) Left ventricular volume and mass from single-plane cineangiocardiogram. A comparison of anteroposterior and right anterior oblique methods. Am Heart J 80:343–352

12. Teicholz L, Kreulen T, Herman M et al (1976) Problems in echocardiographic-angiographic correlations in the presence or absence of asynergy. Am J Cardiol 37:7–11

13. Gorcsan J, Tanaka H (2011) Echocardiographic assessment of myocardial strain. J Am Coll Cardiol 58:1401–1413. https://doi.org/10.1016/j.jacc.2011.06.038

14. Urheim S, Edvardsen T, Torp H, et al (2000) Myocardial strain by Doppler echocardiography: Validation of a new method to quantify regional myocardial function. Circulation 102:1158–1164. https://doi.org/10.1161/01.CIR.102.10.1158

15. Gorcsan J, Gulati VK, Mandarino WA, Katz WE (1996) Color-coded measures of myocardial velocity throughout the cardiac cycle by tissue Doppler imaging to quantify regional left ventricular function. Am Heart J 131:1203–1213. https://doi.org/10.1016/S0002-8703(96)90097-6

16. Sade LE, Gorcsan J, Severyn DA, et al (2005) Usefulness of angle corrected tissue doppler to assess segmental left ventricular function during dobutamine stress echocardiography in patients with and without coronary artery disease. Am J Cardiol 96:141–147. https://doi.org/10.1016/j.amjcard.2005.03.036