Review Article

Strain Echocardiography in Patients with Diastolic Dysfunction and Preserved Ejection Fraction: Are We Ready?

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Abstract

The study of diastolic function in echocardiography has the following primary tasks: 1) Recognizing/categorizing diastolic dysfunction and 2) identifying signs of increased left ventricular filling pressures. The ASE 2016 guideline for the evaluation of left ventricular diastolic function opens possibilities for the use of new technologies that support the diagnostic process. A literature review on the clinical evidence and on the applicability of parameters of strain echocardiography in the evaluation of diastolic function in patients with preserved ejection fraction was carried out.

Introduction

The study of diastolic function in the echocardiography has the following primary tasks: 1) Evaluation/categorization of diastolic dysfunction and 2) recognition of signs of increased left ventricular filling pressures.[1]

When traditional echocardiographic criteria are used alone to diagnose and categorize diastolic dysfunction, they are not sufficiently accurate and therefore several parameters are required to characterize it.[1-3]

However, it is known that this classification format has a prognostic implication: Schillaci et al.[4] demonstrated that the pattern of altered relaxation increases the risk of cardiovascular events in a population of 1839 patients with 11-year follow-up hypertension. Bella et al.,[5] found that the pattern of altered relaxation doubled the risk of mortality, while pseudonormal/restrictive pattern tripled the risk of cardiovascular mortality.

These two studies seem to have been the starting point for Nishimura and Tajik[6] to reconcile the current information and to publish, in 1997, a simplified approach to classify diastolic dysfunction based on Doppler patterns.

The ASE 2016 guideline for the evaluation of left ventricular diastolic function classifies as indeterminate (inconclusive study) those patients presenting 50% positivity of parameters: septal e’ < 7 cm/s and/or lateral e’ < 10 cm/s, average E/e’ ratio > 14, maximum tricuspid regurgitation rate > 2.8 m/s. Consequently, the development of new technologies such as speckle tracking echocardiography (STE) gains space with promising new indexes that expand the possibilities for the evaluation of diastolic function. The guideline brings STE as a supplementary method.[1]

This study aims at reviewing the literature for the use of strain echocardiography parameters in the evaluation of diastolic function in patients with preserved ejection fraction.

Methodology: A literature review was conducted on papers published on PubMed. The MeSH terms used were: diastolic dysfunction, strain, strain rate, speckle tracking echocardiography. By reviewing abstracts, any articles that did not address the subject have been excluded. In addition to that, we did a similar search using the Mendeley application.

Left ventricular radial strain/strain rate

Radial ventricular strain occurs perpendicular to the epicardium, pointing outwards in relation to the ventricular cavity. Using Doppler Tissue Imaging (DTI), Wakami et al.,[7] were the first to study the role of radial strain in diastole and found that the peak left ventricular radial strain during the rapid filling phase had a significant correlation with the tau constant and independent of left ventricular systolic function (Figure 1). Moreover, the peak radial strain during the rapid filling phase was progressively smaller where there was worsening of diastolic dysfunction assessed by transmitral Doppler patterns.

Using STE, Tin tang et al.,[8] found reduced radial strain systolic peak during the resting and exertion phase in patients with heart failure and preserved ejection fraction (HF$_p$EF). Nguyen et al.,[9] also reported reduced levels of radial systolic peak strain rate in individuals with HF$_p$EF.

Kosmala et al.[10] looked for a relationship between radial strain and heart failure symptoms in a hypertensive population. Interestingly, normal or even increased radial peak strain rate (lateral and/or posterior segments) have been found in a NYHA I patient, while reduced rates were found in all myocardial segments in patients with NYHA III and IV heart failure.

Left ventricular longitudinal strain/strain rate

Longitudinal strain is perpendicular to the radial axis towards the left ventricular base. Several authors have studied its use in the evaluation of diastolic function: Wang et al.[11] found that the global peak strain rate in the isovolumetric relaxation phase (Global SRIVR) is related to the tau constant

Keywords

Echocardiography, Doppler; Heart Failure; Diastole,/physiopathology; Ventricular Function/physiopathology; Specklr Tracking; Left Ventricular Dysfunction.

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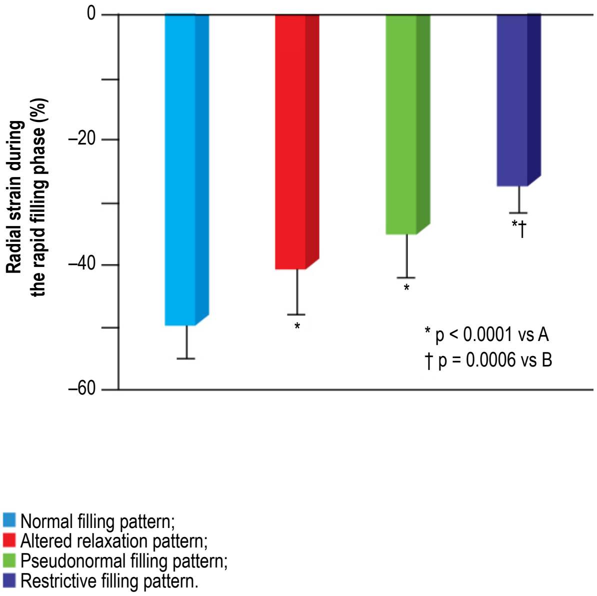


Adapted from Wakami et al.

Figure 1 – *Significant differences in strain values were shown for different filling patterns.*[7]

(τ) and suggests the E/SRIVR ratio for accurate assessment of left ventricular filling pressures.

Del Castillo et al.[12] found that early diastolic strain rate cutoff (peak SR in the rapid filling phase) < 1 would suggest diastolic dysfunction with good sensitivity and high specificity, suggesting that the strain parameter could be used to reclassify cases of undetermined diastolic function. In the same study, the author also evidenced a progressive reduction of this parameter in individuals with more severe diastolic dysfunction.

Hayashi et al.,13 in an elegant study using invasive hemodynamic evaluation for comparative analysis between the tau constant and mean left ventricular diastolic pressure, found the superiority of the E/Global Longitudinal Strain (E/GLS) wave ratio to estimate left ventricular filling pressures with 72% sensitivity and 88% specificity, establishing 680 cm/s as a cutoff value. This parameter presented better accuracy than the E/A ratio and even the E/e' ratio (Figure 2).

Although evidence in many studies points to a linear relationship between left ventricular strain and tau (τ), Bhatia et al.[14] suggest that GLS may not be an appropriate index to discriminate the different stages of diastolic dysfunction.

Based on information from the studies included in this review, GLS alteration appears to occur when there is an increase in left ventricular filling pressures and/or in more advanced degrees of left ventricular diastolic dysfunction (Figure 3).

Left ventricular strain/circumferential strain rate and twist and untwist

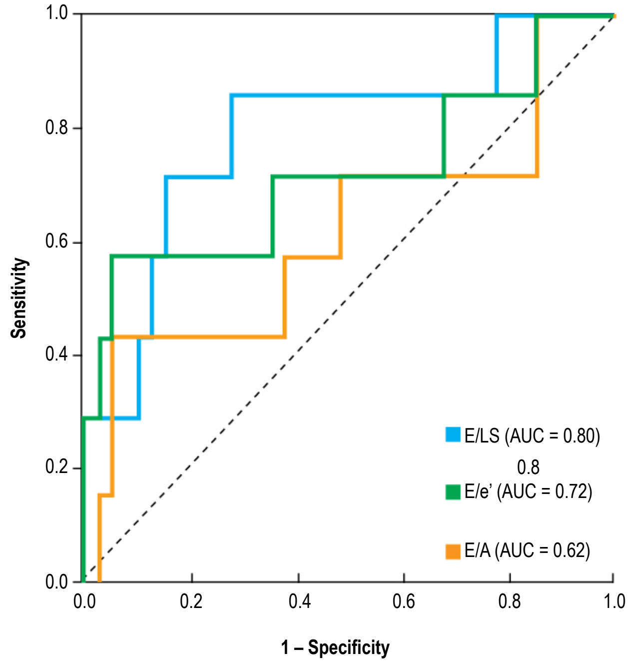
Circumferential strain is perpendicular to the radial and longitudinal axes and is directed counterclockwise around the classic left ventricular short axis. Little has been studied about the Global Circumferential Strain (GCS) in the evaluation of diastolic function.

Differently, ventricular global twist derives from the circumferential-longitudinal shear strain, which mathematically means that the spatial integral of the longitudinal-circumferential shear strain from the base to the apex is equal to the global ventricular torsion. Different groups have focused their interest on the study of left ventricular twist and unstwist. Assuming that 40% of ventricular filling occurs in the isovolumetric relaxation time (IVRT), some authors have proposed the untwisting peak at this stage as a marker of ventricular filling: Bruns et al.[15] suggest it as an early marker of diastolic dysfunction, although the group of Park et al.[16] has shown its greater value in changes during increased loads in the stress test.

The latter has also demonstrated that systolic torsion and diastolic twist are significantly increased in discrete diastolic dysfunction while showing normal and reduced levels in patients with advanced diastolic dysfunction with signs of increased filling pressures.[17]

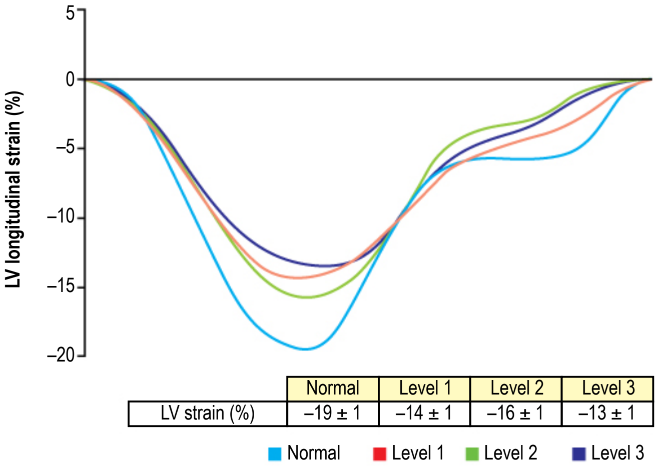
Wang et al.[18] studied twist peak as well as peak untwist rate and did not find any significant differences in control patients and patients with left ventricular diastolic dysfunction (Figure 4). The authors also found that the untwist strain rate was determined primarily by left ventricular twist and end-systolic volume. These findings suggest that twist and untwist rate are compensating factors to maintain ventricular filling and, therefore, would not be the main determining mechanisms in the genesis of HF$_{P}$EF symptoms.

The same group led by Sherif Nagueh, in a subsequent publication,[19] detected that circumferential strain and twist could be preserved when there is abnormal radial and longitudinal strain in a patient with HF$_{P}$EF.



Adapted from Hayashi et al.

Figure 2 – *Comparative evaluation of accuracy to identify increased left ventricular filling pressures: the E/GLS ratio shows a larger area under the curve regarding the E/e' and E/A parameters.*[13]



	Normal	Level 1	Level 2	Level 3
LV strain (%)	–19 ± 1	–14 ± 1	–16 ± 1	–13 ± 1

Adapted from Singh et al.

Figure 3 – *Left ventricular strain curves for the different degrees of diastolic dysfunction.*[26]

Despite all the aforementioned studies, we should not forget the technical difficulties of echocardiographic apical views, which has great variability in the methodology used by the authors.[15-20]

Left atrial strain/strain rate

Left atrial reservoir phase is measured by the atrial wall stiffness and the extent of left ventricular base descent towards the apex.

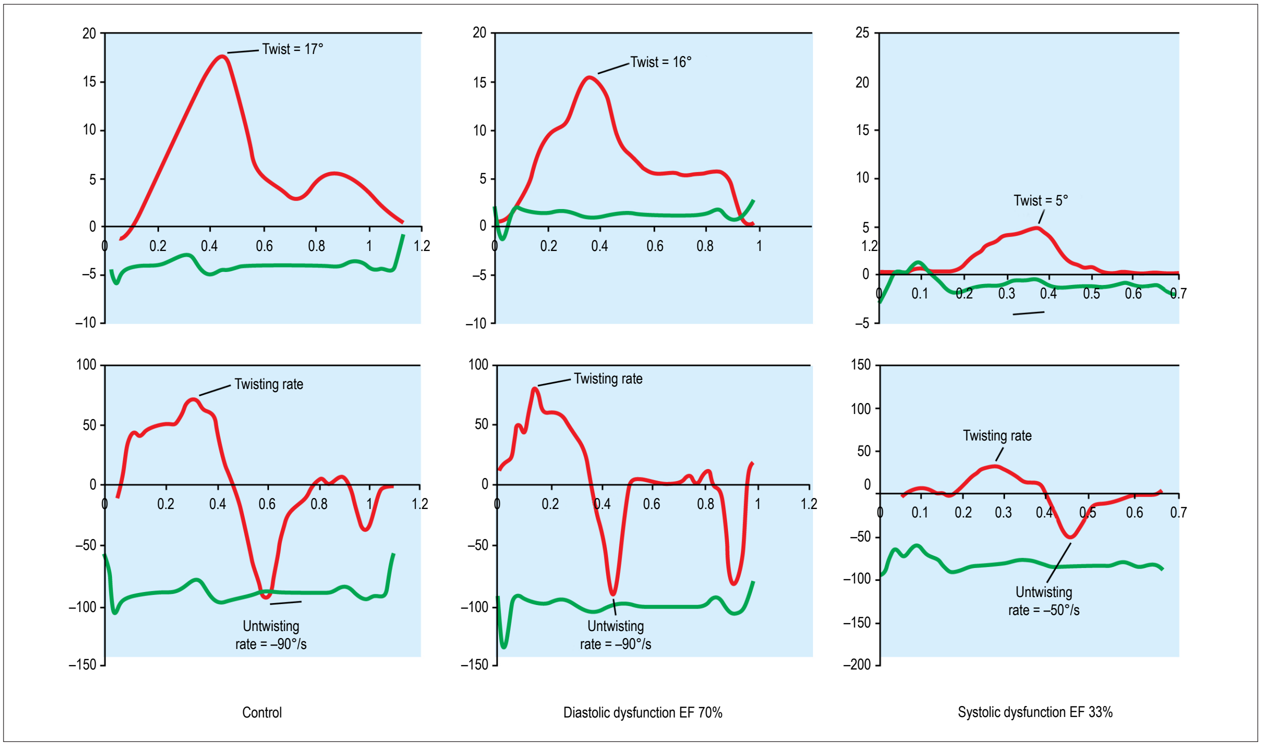


Figure 4 – *Left ventricular twist behavior (upper frames) and left ventricular untwisting rate (lower frames) in three different scenarios: normal individual (left frames), diastolic dysfunction with normal ejection fraction (central frames)and reduced ejection fraction (right frames). Note that there are no significant differences between normal patients and patients with left ventricular diastolic dysfunction.*

There are questions about the additional value provided by the left atrial strain (LA strain) compared to information provided by the GLS and by increased left atrial volume.[21]

However, some considerations seem to indicate an additional LA strain diagnostic value: the classic atrial pressure curves extensively studied in animal and human models, as well as the pulmonary artery catheter, distinguish the passive atrial component (v wave) from the atrial contraction (a wave), from the descent resulting from the left ventricular base (collapse x), as well as descent y, mainly resulting from atrial emptying. If we consider the striking similarity of the classic pressure curves with those of atrial strain, we have evidence of specific atrial components to be assessed and validated for the study of diastolic function.

Macruz proposed that structural left atrial alterations triggered by systemic arterial hypertension should necessarily precede left ventricular alterations.[21] Similar findings using STE were evidenced by Kokubu et al.[22] and Cameli et al.[23], who showed a progressive worsening of strain rate and LA strain values in hypertensive patients with diastolic dysfunction even before left atrial enlargement.

Kurt et al.[24] proposed atrial stiffness index using the ratio between the E/e' and LA strain parameters. Comparing to the pulmonary artery wedge pressure, a cut-off value of 1.1 mmHg was established, showing 84% sensitivity and 100% specificity to distinguish patients with heart failure from patients with diastolic dysfunction without heart failure. Khan et al.[25] found that the atrial stiffness index was also significantly higher among patients with diastolic dysfunction compared to controls.

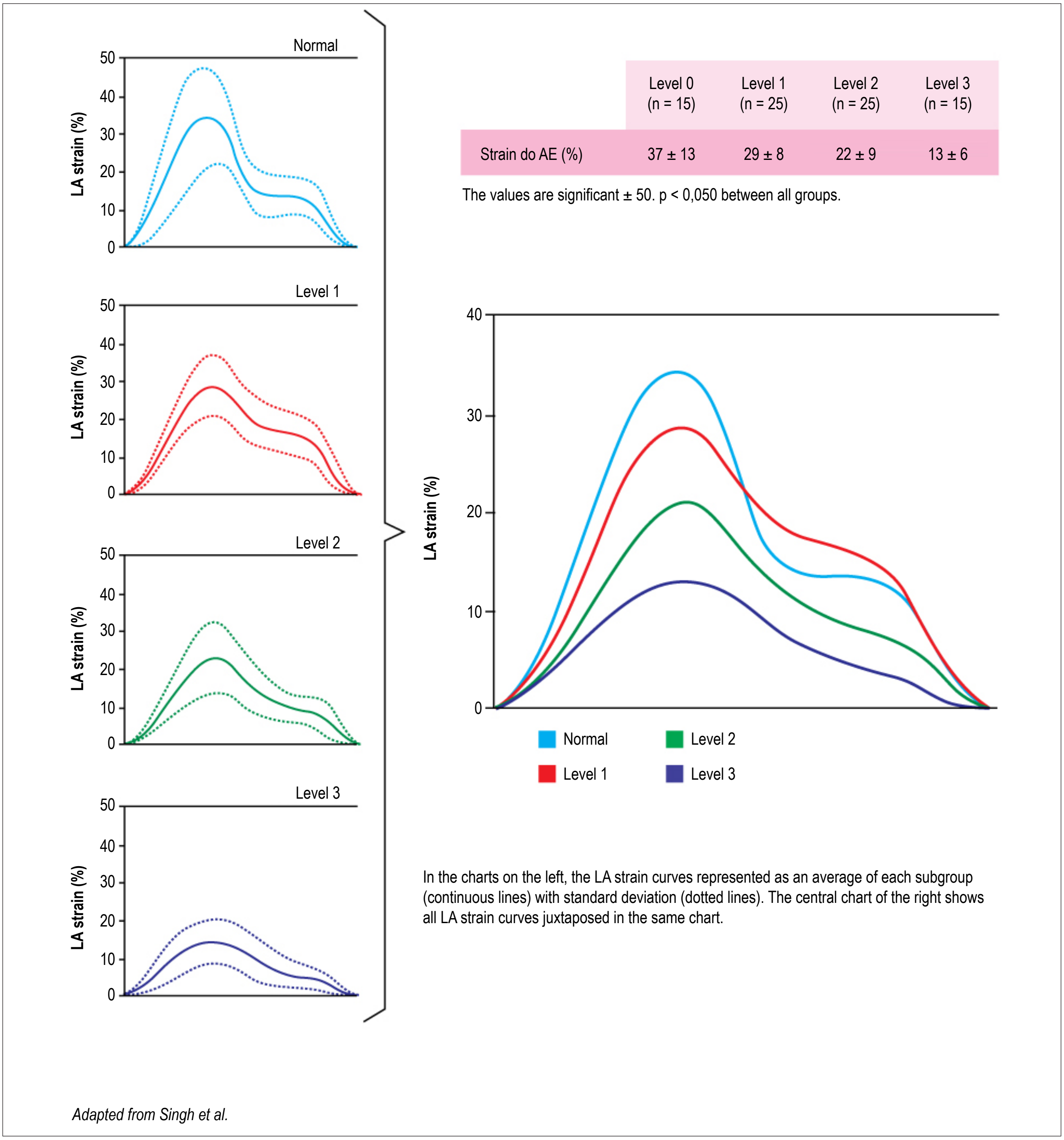
Singh et al.[26] found that all three atrial function phases were affected with worsening diastolic dysfunction degree. The reservoir phase deteriorates with worsening diastolic dysfunction with significant reduction occurring between grades 1 and 2 versus normal. Conduit function behaves similarly. Interestingly, the atrial contraction phase initially increases in grade I diastolic dysfunction and reduces in subsequent stages. This finding was also reproduced by Brecht et al.[27] (Figure 5).

Unlike the left ventricle, left atrial evaluation using STE was not validated by sonomicrometry and/or myocardial tagging with magnetic resonance imaging, but the number of evidences that surfaced in the last decade supports its diagnostic and prognostic value.

Diastole as an integral part of the cardiac cycle

Ventricular filling is a complex phenomenon involving multiple physiological variables and is closely related to the other phases of the cardiac cycle. The ideal number of parameters for the best characterization of diastolic function is still an unresolved issue.[3]

In this review, it is evident that strain echocardiography has provided a growing body of evidence supporting its use in the evaluation of left ventricular diastolic function. LA strain emerges as a parameter that may help categorizing diastolic dysfunction and estimation of left ventricular filling pressures, whereas GLS seems to change only in the latter scenario. Obviously, further studies are needed to formalize the routine employment of both.



	Level 0 (n = 15)	Level 1 (n = 25)	Level 2 (n = 25)	Level 3 (n = 15)
Strain do AE (%)	37 ± 13	29 ± 8	22 ± 9	13 ± 6

The values are significant ± 50. p < 0,050 between all groups.

In the charts on the left, the LA strain curves represented as an average of each subgroup (continuous lines) with standard deviation (dotted lines). The central chart of the right shows all LA strain curves juxtaposed in the same chart.

Adapted from Singh et al.

Figure 5 – *Left atrial strain curves for different degrees of diastolic dysfunction.*[26]

In an editorial on Singh's article, Solomon and Biering-Sørensen[28] provide some criticism of LA strain: "it remains uncertain whether the peak strain of the reservoir phase actually assesses the intrinsic properties of the left atrium and diastolic dysfunction besides longitudinal left ventricular displacement. Nevertheless, left atrial complacency measurement can definitely be useful in assessing HFpEF."

The ASE 2016 guideline for the evaluation of left ventricular diastolic function proposes the E/e′ ratio to estimate filling pressures,[1] although this parameter is questioned as to its actual accuracy for this purpose.[2,3] The E/e′ ratio can be seen, from a hemodynamic point of view, as a pressure-volume ratio (P/V), since the E wave estimates the diastolic pressure gradient LA-LV, whereas the e′ wave infers the global left ventricle volumetric variation from the analysis of its basal segments during the rapid filling phase.

Consequently, both the substitution of e′ for GLS in the attempt to find a denominator closer to global volumetric variation[13] and the correction of the pure E/e' by LA strain AE[24] show a physiological rationale for a more accurate evaluation of filling pressures. More extensive studies are required to evaluate, compare and validate these indexes.

With regards to ventricular strain and its evaluation in different cardiac axes, it can be inferred that it is possible to identify states of abnormality that result in hypofunction of one of the cardiac axes and compensatory hyperfunction in the other axes: DeVore et al.[29] detected GLS impairment in 65% of the individuals with HF_pEF. However, there was no association between GLS values and symptoms, quality of life or functional capacity.

Stokke et al.[30] have recently used a mathematical model to find out how the reduction of longitudinal shortening can be compensated as to keep the ejection fraction unchanged: each reduction of 1 percentage point in longitudinal shortening can be compensated with an increase of 0.5 percentage points in circumferential shortening, an increase of roughly 0.9 mm in wall thickness or a 6-9 mL reduction in end diastolic volume.

This allows us to provide important information about the interdependence of anatomical parameters and of these with functional variables of the cardiovascular system. In addition, it shows us how intricate are the concepts of systolic and diastolic function in the dialectics of the heart as a pressing pump.

Borg and Ray,[31] in an excellent editorial on the article by Park et al.,[32] propose a unified network of parameters to explain different manifestations of heart failure and the progression of pathological states incorporating ventricular restoration forces, remodeling and torsion (Figure 6).

Finally, the emergence of new technologies that show other aspects of the heart physiology (ultrafast imaging) and the implementation of the practice of artificial intelligence techniques (machine learning) in the establishment of "precision cardiology" can provide a deeper understanding of echocardiographic evaluation of ventricular function.[33,34]

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Authors' contributions

Research creation and design: Hortegal R, Abensur H; Data acquisition: Hortegal R, Abensur H; Data analysis and interpretation: Hortegal R, Abensur H; Manuscript drafting: Hortegal R, Abensur H; Critical revision of the manuscript as for important intellectual content: Abensur H.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

Sources of Funding

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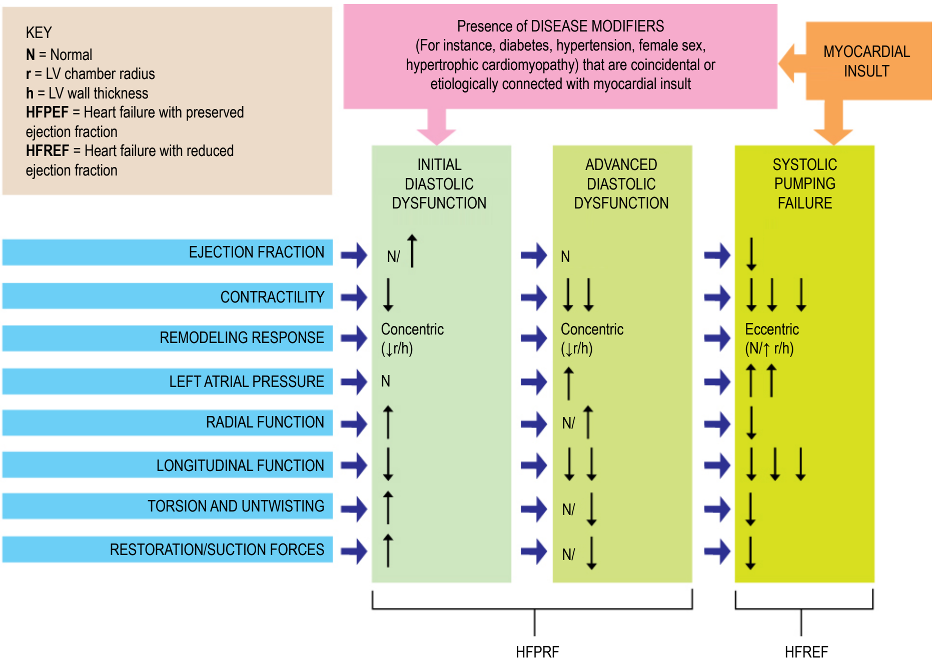
Academic Association

This study is not associated with any graduate programs.



KEY
N = Normal
r = LV chamber radius
h = LV wall thickness
HFPEF = Heart failure with preserved ejection fraction
HFREF = Heart failure with reduced ejection fraction

	INITIAL DIASTOLIC DYSFUNCTION	ADVANCED DIASTOLIC DYSFUNCTION	SYSTOLIC PUMPING FAILURE
EJECTION FRACTION	N/ ↑	N	↓
CONTRACTILITY	↓	↓ ↓	↓ ↓ ↓
REMODELING RESPONSE	Concentric (↓r/h)	Concentric (↓r/h)	Eccentric (N/↑ r/h)
LEFT ATRIAL PRESSURE	N	↑	↑ ↑
RADIAL FUNCTION	↑	N/ ↑	↓
LONGITUDINAL FUNCTION	↓	↓ ↓	↓ ↓ ↓
TORSION AND UNTWISTING	↑	N/ ↓	↓
RESTORATION/SUCTION FORCES	↑	N/ ↓	↓

Adapted from Borg et al.

Figure 6 – *Unified network of parameters to explain different manifestations of heart failure and the progression of pathological states incorporating ventricular restoration forces, remodeling and torsion.*[31]

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