Review Article

Applications of Strain and Strain Rate in the Evaluation of Left Ventricular Diastolic Function

José Maria Del Castillo[1,2], Carlos Mazzarollo[1,2], Waldemiro Carvalho[1,3], Jonny Vitor Diniz[1,2], Katarina Barros Oliveira[1,2], Deborah Costa Lima Araujo[1,2], Eugenio Soares Albuquerque[1,2]
[1]Escola de Ecografia de Pernambuco, Recife, PE; [2]Universidade Católica de Pernambuco, Recife, PE; [3]Hospital de Messejana, Fortaleza, CE – Brazil

Abstract

The analysis of diastolic function using conventional echocardiography (two-dimensional method, spectral Doppler and tissue Doppler) may not determine some cases of diastolic dysfunction or high left atrial pressure. The parameters that study myocardial strain (left atrial strain rate and longitudinal strain) may help diagnosis. This study describes the diastolic strain rate methods during isovolumetric relaxation time and at peak filling, apical twisting rate and maximal longitudinal left atrial strain, analyzing their applications and advantages.

Introduction

Abnormalities in ventricular, systolic and diastolic function play an important role among the factors that determine the prognosis of cardiovascular diseases. It has also been found that patients with preserved diastolic dysfunction and ejection fraction (EF) present unfavorable evolution as well as patients with depressed EF.[1] In order to understand the current state of the recommendations on diastolic dysfunction, it is necessary to divide patients into two large groups: normal left atrial pressure (LAP), which is the lighter form, and increased LAP, in which patients are more symptomatic and have a worse prognosis.[2]

Ventricular function is a consequence of the mechanisms that regulate myocardial contractility, determined by the heart's helical shape, which generates the twisting and untwisting movements.[3] Systolic and diastolic ventricular functions are closely interrelated, working the myocardium during the cardiac cycle, in a continuous and uninterrupted manner. We found, as a normal myocardial function, the one that maintains adequate cardiac output in all conditions of activity, leaving the filling and emptying pressures of the cavities within normal limits, according to the patient's age and the physiological conditions to which the patient is accustomed. The conditions of normality differ between young, elderly, sedentary and non-sedentary patients.

Keywords

Ventricular Dysfunction; Strains; Systolic Pressure; Diastolic Pressure.

Mailing Address: José Maria Del Castillo •
Rua Jorge de Lima, 245, apto. 303, Salute, Imbiribeira. CEP: 51160-070, Recife, PE – Brazil.
E-mail: castillojmd@gmail.com

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The diastolic function is that which regulates ventricular filling, which initially occurs by the untwisting mechanism, in which the contraction of the ascending segment of the ventricular apical band tends to distort the ventricle, promoting a rapid drop in intraventricular pressure without volume change (Isovolumetric Relaxation Time — IVRT), creating a negative pressure gradient between the base and the apex of the Left Ventricle (LV).[4] The decrease in intraventricular pressure between the closure of the aortic valve and the opening of the mitral valve occurs linearly according to time, known as the tau constant (τ). Once the intraventricular pressure falls below the LAP, the mitral valve opens and the intraventricular negative pressure rapidly sucks the blood contained in the atrial cavity during rapid ventricular filling. At this time, the ventricular myocardium undergoes a process of rapid untwisting. Then, the passive phase of diastole occurs, culminating with atrial contraction, the pressure-volume ratio of which depends on the LV wall complacency. Correlating these observations with the regime of intracavitary pressures, Figure 1 summarizes this ratio.[5]

Diastolic dysfunction, when assessed by conventional Doppler echocardiography, is divided into three types: grade 1 or abnormal relaxation, in which LAP is normal; grade 2 or pseudonormal, in which the mitral flow seems normal, but there are signs of increased LAP; and grade 3, restrictive, in which there are clear signs of increased LAP. The way in which diastolic dysfunction and elevation of LAP cannot be determined is called indeterminate.

The most recent recommendation on diastolic function[6] separates the methods used to measure it in major, secondary, and new indices.

Main echocardiographic methods for assessing diastolic function

Among the main parameters, mitral Doppler flowmetry is the method that should be used first to evaluate diastolic function, but may be insufficient to define the patient's actual situation, and other methods of measurement should often be used. In young adults, mitral Doppler presents, after mitral opening, a rapid increase in the flow velocity (D-E segment), culminating in the E wave. The velocity of this wave, however, decreases significantly with age and is less than 50 cm/s and the E/A ratio is lower than 0.8 in individuals older than 60. In young people, by contrast, the E/A ratio is often higher than 2.0.[7] This means that the age group plays a key role in the analysis of diastolic function.

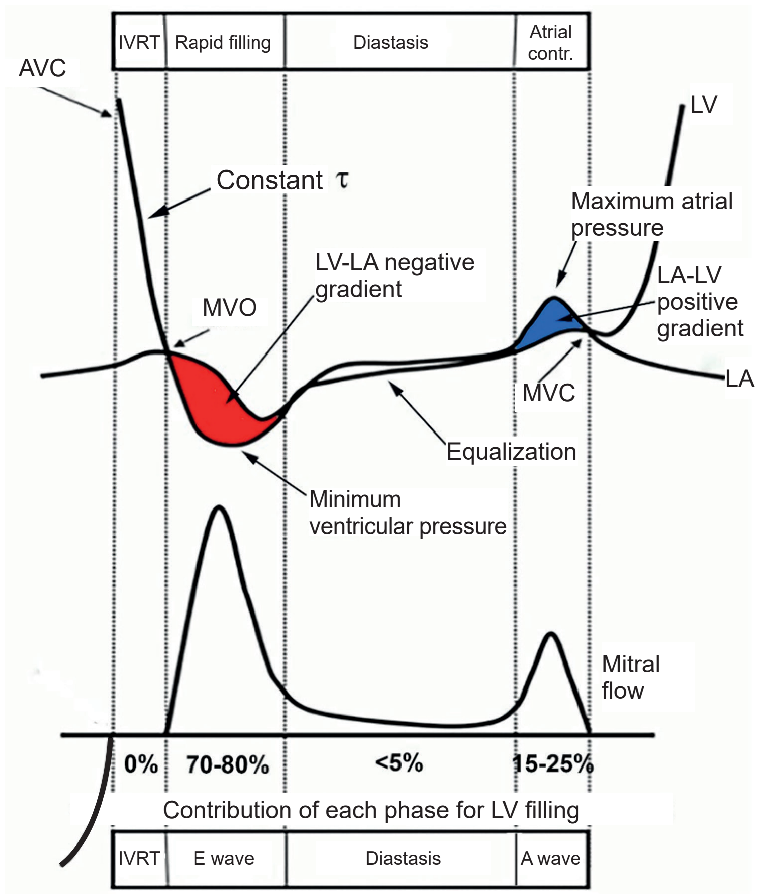

Figure 1 – *Schematic representation of the ventricular diastolic phase. Ventricular and atrial diastolic pressures are observed. In red, the gradient between the left ventricle (LV) and the left atrium (LA), negative, promotes rapid ventricular filling. In blue, the gradient between the LA and LV, positive, completing ventricular filling with the atrial contraction. Diastolic phases and the contribution of each phase to the ventricular filling are observed. AVC: aortic valve closure; MVC: netral valve closure; IVRT: isovolumetric relaxation time. MVO: mitrae valve opening.*

Another major feature used to measure diastolic function is Tissue Doppler (TD) of the mitral annulus, whose wave e′ represents the ventricular untwisting velocity. The velocity is greater in the lateral annulus than in the septal annulus and corresponds to the velocity with which this area moves along the Doppler line.[8] The mitral annulus velocity can be influenced by extrinsic constraints, as in pericarditis, in which the inversion of septal and lateral velocities is observed.[9] According to the current recommendations, the normal values are > 10 cm/s for the lateral annulus and > 7 cm/s for the septal annulus, but these values are disputed because in higher age groups the velocities may be lower. Mitter et al.[10] proposed normal values for the lateral annulus > 10 cm/s for patients younger than 55, > 9 cm/s for patients aged between 55 and 65, and > 8 cm/s for individuals older than 65. The e′ wave velocity must be related to the mitral flow E wave velocity. The current recommendation establishes the following normal values: lateral E/e′ ratio < 13; septal E/e′ ratio < 15; mean E/e′ ratio < 14. Higher values are a sign of increased LAP. The study by Mitter et al. proposes the following ratio: E/e′ ratio < 8 corresponds to the really normal LAP; E/e′ ratio of 8 to 12 indicates undetermined LAP; E/e′ ratio > 12 indicates an increase in LAP.

LA volume is undoubtedly an important indicator of increased atrial, ventricular, diastolic and pulmonary capillary (PCP) pressures. It is the main method for the evaluation of these pressures, according to the current recommendation on diastolic function.[6] Its calibration is easy and the 4-chamber and 2-chamber apical views should be used, at the end of ventricular systole, excluding the atrial appendage and the mouth of the pulmonary veins. Its body surface indexation is critical for the correct analysis. However, there are disagreements as to its limit value. Until the 2009 recommendation, the indexed LA volume considered normal was up to 28 mL/m^2,[7] and volume ≥ 34 mL/m^2 was considered an independent predictor of death, heart failure, atrial fibrillation, and ischemic stroke.[11] In 2015, in the new guideline on quantification of cavities,[12] the normal value was increased to 34 mL/m^2, a criterion followed by the current recommendation on diastolic function. Mitter et al.,[10] however, suggest maintaining the value of 28 mL/m^2 and argue that higher values are associated with diastolic dysfunction. Mitral reflux in patients with or without diastolic dysfunction causes LA dilation and may lead to misinterpretations.

The flow of pulmonary veins is another major measurement. Obtaining the right inferior[13] pulmonary vein flow from the apical 4-chamber position depends on the echocardiographic image quality, since the depth at which the pulsatile Doppler sample volume should be positioned is usually large. Because of this, the image is not often satisfactory. As during the diastole, the pulmonary veins, LA and LV form a communicating chamber, diastolic abnormalities can be measured by this flow. Under normal conditions, the ratio of S/D waves is greater than 1 (S > D) and reverse atrial flow has a velocity <35 cm/s and duration up to 30 ms longer than the mitral A wave duration. In young people, the S/D ratio may be smaller than 1.

Another major parameter considered by the current recommendation on diastolic function[6] is the tricuspid reflux velocity. Due to the increase in LAP and, therefore, PCP, there is an increase in pulmonary vascular resistance, a consequence of reactional pulmonary arteriolar vasoconstriction. This causes right ventricular (RV) remodeling with hypertrophy, dilatation and increased systolic pressure of the cavity and, usually, tricuspid valve reflux, whose velocity corresponds to the systolic pressure gradient between the RV and the Right Atrium (RA). The normal RV pressure is up to 31 mmHg (corresponding to a tricuspid reflux velocity of 2.8 m/s). Higher values, in the presence of LV diastolic dysfunction, are considered indicative of increased LAP. This parameter should be used with caution in the presence of pulmonary disease or valvopathy that may increase pulmonary pressure.

The Valsalva maneuver, another major measure, consists in forcing expiration with the mouth and nose closed for at least 10 seconds and is intended to increase intrathoracic pressure and, as a consequence, decrease the systemic and pulmonary venous return. Reduction of pulmonary venous return causes a decrease in LAP and LV and PCP diastolic pressure. The response should vary according to whether there is diastolic dysfunction or not: normal individuals respond with a global decrease in mitral flow, that is, with an equal decrease in the velocity of waves E and A. Patients with diastolic dysfunction and high LAP should have this pressure decreased, hence improving such dysfunction, which causes reduced E wave velocity and increased A wave, turning into grade 1 dysfunction. The Valsalva maneuver is a good method to reveal diastolic dysfunction with increased LAP, but it has the drawback of its execution in practice: many patients cannot sustain the maneuver for the minimum recommended time, and others cannot even begin the maneuver.

Secondary echocardiographic methods for assessing diastolic function

The intraventricular flow Velocity of Propagation (VP), or color M mode of the LV inflow tract, records the blood flow progression from the mitral annulus to the apex of the cavity during the rapid ventricular filling phase. It responds to a complex mechanism in which the spatial-temporal distribution of intraventricular flow velocity is governed by Euler's hydrodynamic equation,[14] which correlates pressure, space, time and velocity, representing the rapid ventricular filling due to the intraventricular negative pressure caused by helical band untwisting. Its relationship with mitral E-wave (E/VP) > 2.5 in patients with depressed EF correlates reasonably with PCP > 15 mmHg, but should not be used in patients with preserved EF.[6]

Another secondary measure is IVRT, which corresponds to the interval between aortic valve closure and mitral valve opening, in which ventricular untwisting causes a rapid reduction of intracavitary pressure, without volume modification, and generates the so-called constant τ. The determination of IVRT should be performed with continuous Doppler from the 3-chamber or 5-chamber apical positions, placing the Doppler line between the LVOT and the mitral valve, thus simultaneously recording both flows. This time varies considerably with age. Table 1 shows the reference values.

Another secondary method, according to the current recommendation on diastolic function,[6] is the TE-e' interval. This calculation, which identifies PCP > 12 mmHg with 95% sensitivity and 88% specificity in patients with atrial fibrillation, relates the time between the electrocardiogram (ECG) R wave and the beginning of the mitral E wave (ET), which is subtracted from the time between the ECG R wave and the beginning of the mitral annulus tissue Doppler e' wave.[15] The measurement must be very precise, requiring the simultaneous recording of mitral flow Doppler and mitral annulus tissue Doppler, which limits its practical use.

New echocardiographic methods for assessing diastolic function

The new echocardiographic indexes for the detection of diastolic dysfunction use the parameters of myocardial strain and are mentioned in the recommendation as potentially useful, but still without sufficient evidence for its routine use.[6] Normally, patients with diastolic dysfunction and decreased EF have a decreased LV Global Longitudinal Strain (GLS), but because of the dispersion of results, it is not recommended to use this index to detect diastolic dysfunction. Diastolic strain rate during IVRT and early diastolic e' wave strain rate correlates better with diastolic dysfunction and both analyze the ventricular untwisting period. Another potentially useful index is the untwisting rate that is calculated during untwisting or apical LV twisting analysis. LA longitudinal strain which correlates with left atrial pressure, is also mentioned.

Table 1 – Reference values for isovolumetric relaxation time (IVRT) estimated by spectral Doppler.

	Age group, years			
	16-20	21-40	41-60	>60
IVRT, milliseconds	50±9 (32-68)	67±8 (51-83)	74±7 (60-88)	87±7 (73-101)

Source: adapted from Nagueh SF et al. J Am Soc Echocardiogr 2009; 22(2):107.

Strain rate during isovolumetric relaxation time

The strain rate measures the time used to produce myocardial strain, is expressed in s^{-1} and represents the efficiency of the strain. Its determination must be performed during the isovolumetric phase (Figure 2), but it may have the drawback of determining the aortic valve closure, at which point the Strain Rate is calculated during IVRT (SR_{IVRT}).[16] This may partly limit its results, since the aortic closure varies in the different cardiac cycles and in multiple echocardiographic projections, mainly if there is arrhythmia or atrial fibrillation. Its ratio with the mitral E wave (E/SR_{IVRT}) adds sensitivity, but it does not seem to be superior to the E/e′ ratio. In an experimental study performed in dogs, complemented with right catheterization in 50 patients, it was found that SR_{IVRT} showed a strong correlation with constant τ (decrease in intraventricular pressure during the isovolumetric relaxation time), with $r = -0.83$ and $p = 0.001$, and that the E/SR_{IVRT} ratio showed the best correlation with PCP ($r = 0.79$ and $p = 0.001$), being more useful when the mean E/e′ ratio was between 8 and 15, considered intermediate or indeterminate.[17] A recent intraoperative study in patients who underwent coronary artery bypass grafting, comparing PCP with strain rate during IVRT (SR_{IVRT}), showed that SR_{IVRT} was superior to the E/e′ ratio to estimate PCP > 15 mmHg (Receiver Operating Characteristic Curve — ROC 0.94 vs. 0.47).[18]

Early diastolic strain rate

The strain rate obtained at peak e′ wave is easier to obtain but appears to correlate less efficiently with diastolic dysfunction than SR_{IVRT}. Its ratio with the mitral E wave (E/early diastolic strain rate — SRe) also shows results not higher than those obtained with the E/e′ ratio (Figure 2).[16]

In a recent study,[19] SRe lower than 1.0 s^{-1}, using the ROC statistical method, Area Under the Curve (AUC) of 0.95, $p < 0.0001$, separated with good sensitivity (83.9%) and excellent specificity (100%), normal individuals of patients with different grades of diastolic dysfunctions, allowing to reclassify 92% of patients with undetermined diastolic dysfunction into normal diastolic function (48%), diastolic dysfunction grade 1 (40%) and diastolic dysfunction grade 2 (4%), with 8% remaining in the indeterminate form.

A study with patients with acute myocardial infarction with a 29-month follow-up showed that an E/SRe ratio > 1.25 correlated with a higher rate of post-infarction complications, such as death, heart failure, stroke and atrial fibrillation, also pointing out that when clinical data, E/e′ ratio and mitral deceleration time < 140 ms were added, the incremental value of the method was highly significant.[20] Another study with 120 patients with coronary artery disease and preserved LV systolic function undergoing elective coronary artery bypass grafting, correlating diastolic strain rate with PCP determined by Swan-Ganz™ pulmonary artery catheter showed that the diastolic strain rate at the mitral E-wave peak (E/SRd ratio) ≥ 1.2 presented high specificity and sensitivity (100% and 96.63%, respectively; AUC 0.99) to predict PCP > 15 mmHg. In the same study, the correlation E/e′ ≥ 13 presented 74.19% sensitivity and 75.28% specificity with AUC 0.84.

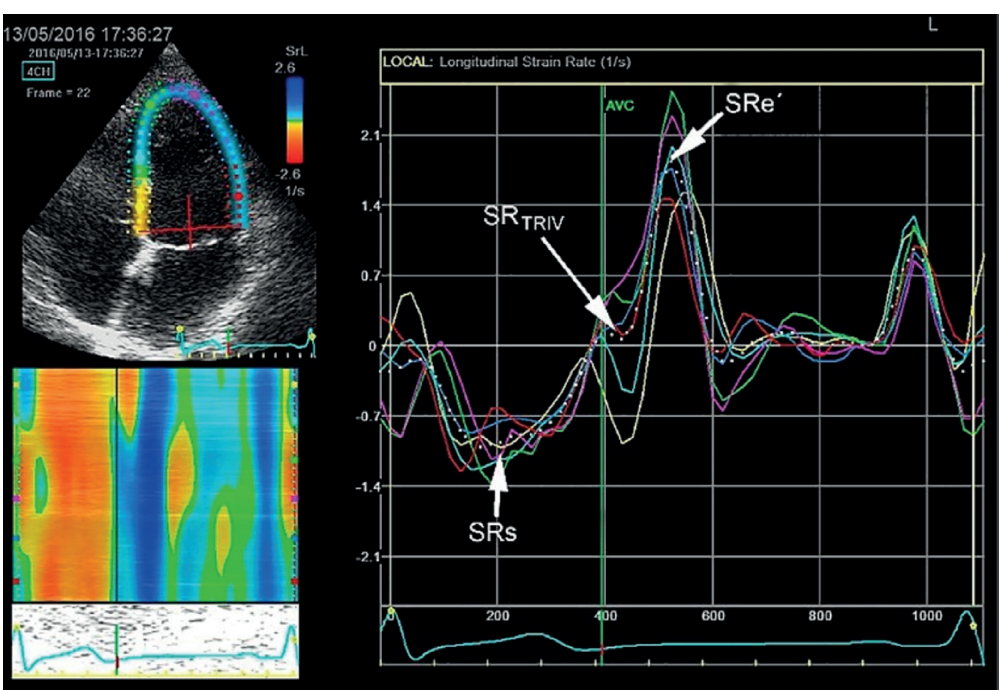

Figure 2 – *Determination of strain rate from the 4-apical chamber position. The image reveals the following components: systolic strain rate (SRs), strain rate during isovolumetric relaxation time (SRIVRT), early diastolic strain rate (SRe′). AVC: aortic valve closure.*

Untwisting rate and untwisting time

This index measures the Untwisting Rate ($SR_{untwist}$) the same way the strain rate measures the strain. The reference values are estimated in degrees/s^{-1}, with normal values in healthy individuals of -91±18 °/s^{-1}.[22] $SR_{untwist}$ precedes other variables such as intraventricular gradient peak and rapid ventricular filling peak. Any condition affecting $SR_{untwist}$ can also affect diastolic filling, end diastolic volume and ejection volume.[23] Untwisting time seems to correlate better with diastolic dysfunction in patients with preserved EF.[24] Comparison of $SR_{untwist}$ with myocardial velocities shows that $SR_{untwist}$ precedes the velocities (Figure 3).[25] This methodology is only present in some equipment, which makes it difficult to apply it in practice.

Left atrial longitudinal strain

Some studies have shown a correlation between the LA Longitudinal Strain (LS_{LA}) reduction in the reservoir phase (maximum strain) and LAP increase.[26,27] The correlation between the E/e' ratio and the LS_{LA} in patients with chronic myocardiopathy in the chronic phase of the Chikungunya virus infection, with decreased longitudinal LA strain related to an increase in the E/e' ratio has been found (Figure 4).[28]

A study of 229 cases, including controls and patients with different grades of diastolic dysfunction, analyzed the LA and LA_{LA} volumes and showed that the indexed LA volume gradually increased in grades of diastolic dysfunction, but did not separate patients with grade 1 from grade 2 diastolic dysfunction. The LS_{LA}, in the reservoir phase (maximum longitudinal strain), showed different cutoff values to detect the different grades of diastolic dysfunction, better separating the patients.[29] (Table 2)

A recent updated review on the evaluation of LA function by longitudinal strain and volumetric measurements (expansion index, total emptying fraction and active LA emptying fraction) shows that the strain methods correlate better with clinical cardiovascular events than with dynamic volumetric methods (atrial function) and static volumetric methods (volume index and LA dimension), even when these data are not altered yet.[30]

Conclusion

The analysis of ventricular diastolic function using conventional methods of analysis (two-dimensional echocardiography, spectral Doppler and tissue Doppler) is useful to diagnose diastolic dysfunction in most cases, provided that a thorough and systematic analysis is performed using all echocardiographic resources. However, some patients are considered intermediate or indeterminate, either in determining the diastolic dysfunction grade or the diagnosis of high left atrial pressure, especially those with preserved ventricular function. In these cases, the evaluation of strain and strain rate can be very useful in the classification and/or identification of diastolic dysfunction and elevation of left atrial pressure. An increasing number of studies corroborate the usefulness of cardiac strain and, especially, diastolic strain rate, in the identification of these dysfunctions. An important role is played by the left atrial longitudinal strain, whose pathophysiology has been intensively studied.

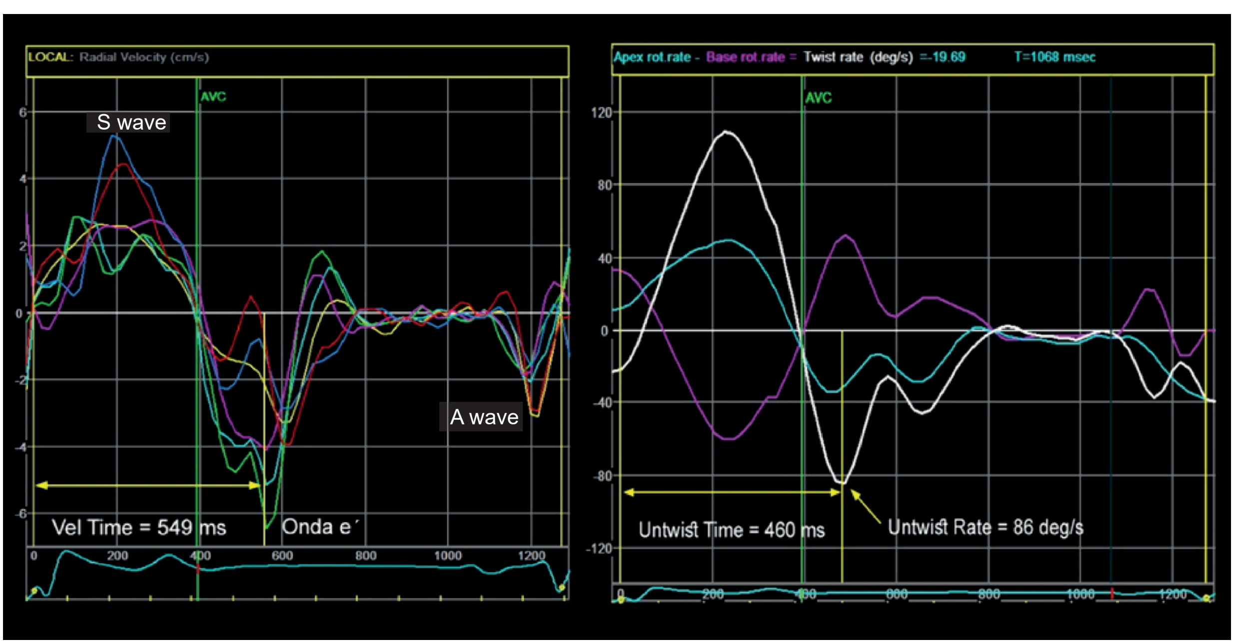

Figure 3 – *Left ventricular radial velocity (left) and twisting rate (to the right) during systole and initial diastole in normal individuals at rest in the same cardiac cycle. In the velocity image, the left ventricular filling velocity time (Vel Time) is significantly greater than the untwist time, revealing that the untwisting time precedes the myocardial velocity. AVC: aortic valve closure.*

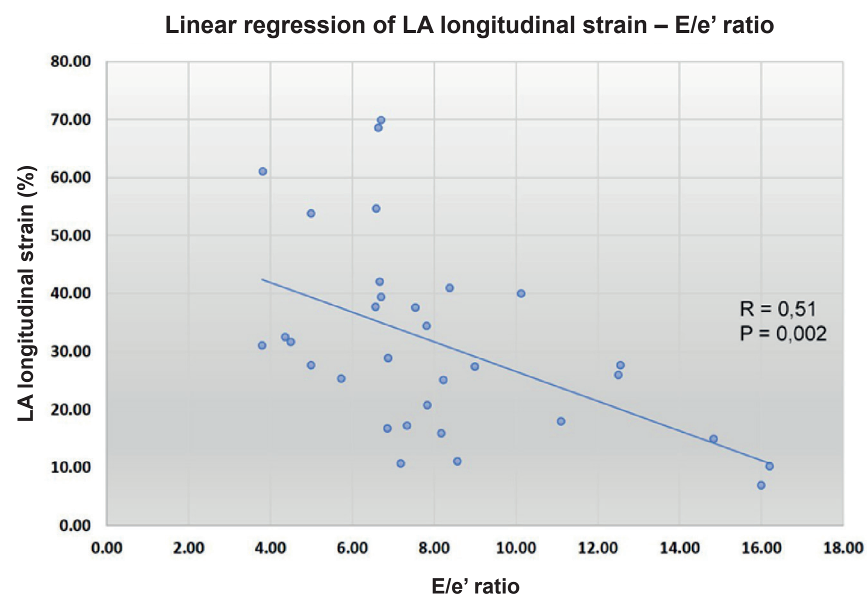

Figure 4 – *Linear regression curve between left atrial (LA) strain and E/e' ratio of mitral flow and tissue Doppler, showing a decrease in LA longitudinal strain with increased E/e' ratio.*

Table 2 – Analysis of area under the curve (AUC) for left atrial longitudinal strain in the validation of groups using the 2009 diastolic function guideline.

By-group			Validation group				
	AUC	Cut-off value (%)	Sensitivity	Specificity	PPV	NPV	Precision
Grade 0 vs. grade 1-3	0,86	35	90	59	61	90	72
Grade 0-1 vs. grade 2-3	0,89	24	75	92	75	92	88
Grade 0-2 vs. grade 3	0,91	19	90	95	64	99	95

PPV: positive predictive value; NPV: negative predictive value. Source: adapted from Singh et al., JACC Cardiovasc Imaging 2017; 10:735).

Authors' contributions:

Research creation and design: Castillo JMD; Data acquisition: Castillo JMD, Mazzarollo C, Carvalho W, Oliveira KB, Araujo DCL e Albuquerque ES; Diniz JV; Data analysis and interpretation: Castillo JMD, Diniz JV; Manuscript writing: Castillo JMD; Critical revision of the manuscript for important intellectual content: Castillo JMD e Diniz JV.

Potential conflict of interest

The authors declare that there is no relevant conflict of interest.

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