Myocardial Deformation by Speckle Tracking in Severe Dilated Cardiomyopathy

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Abstract

Background: The high and increasing prevalence of Dilated Cardiomyopathy (DCM) represents a serious public health issue. Novel technologies have been used aiming to improve diagnosis and the therapeutic approach. In this context, speckle tracking echocardiography (STE) uses natural myocardial markers to analyze the systolic deformation of the left ventricle (LV).

Objective: Measure the longitudinal transmural global strain (GS) of the LV through STE in patients with severe DCM, comparing the results with normal individuals and with echocardiographic parameters established for the analysis of LV systolic function, in order to validate the method in this population.

Methods: Seventy-one patients with severe DCM (53 ± 12 years, 72% men) and 20 controls (30 ± 8 years, 45% men) were studied. The following variables were studied: LV volumes and ejection fraction calculated by two and three-dimensional echocardiography, Doppler parameters, Tissue Doppler Imaging systolic and diastolic LV velocities and GS obtained by STE.

Results: Compared with controls, LV volumes were higher in the DCM group; however, LVEF and peak E-wave velocity were lower in the latter. The myocardial performance index was higher in the patient group. Tissue Doppler myocardial velocities (S', e', a') were significantly lower and E/e' ratio was higher in the DCM group. GS was decreased in the DCM group (-5.5% ± 2.3%) when compared with controls (-14.0% ± 1.8%).

Conclusion: In this study, GS was significantly lower in patients with severe DCM, bringing new perspectives for therapeutic approaches in this specific population. (Arq Bras Cardiol 2012;99(3):834-842)

Keywords: Cardiomyopathy; dilated / physiopathology; echocardiography; Doppler; ventricular dysfunction, left.

Introduction

In recent years, novel technologies have appeared to improve diagnosis and treatment of heart diseases. In this context, speckle tracking echocardiography (STE) is useful to detect and comprehend the abnormalities that occur in cardiac diseases. STE is based on the tracking of natural myocardial markers during the cardiac cycle[1,2].

Dilated Cardiomyopathy (DCM), which usually culminates in congestive heart failure (CHF) and death, represents a severe public health issue, as population ageing, associated with morbidity and mortality of this disease requires effective therapeutic approaches. It is well established in literature that endocardial fibers, arranged longitudinally, are the first to undergo damage in DCM[3]; thus, myocardial deformation (strain) that occurs in the longitudinal plane is the first to express these alterations[4].

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The present study aims to clinically validate the use of longitudinal transmural strain, obtained through speckle tracking, to assess left ventricular systolic function in patients with severe DCM, by comparing them with normal individuals and with already established echocardiographic parameters.

Methods

Seventy-one consecutive patients with severe DCM were prospectively analyzed in this protocol, according to the following inclusion criteria: left ventricular ejection fraction (LVEF) < 35%, measured according to modified Simpson's rule and transthoracic echocardiogram suitable for detection and tracking of speckles. The exclusion criteria were age < 18 and > 75 years; recent episode (<1 month) of ventricular fibrillation; atrial fibrillation; concomitant diseases determining a poor prognosis (e.g., cancer), patients who refused to participate in the study; severe primary valvular disease with significant hemodynamic effect. Twenty healthy volunteers comprised the control group.

All patients gave written informed consent, and the study was approved by Sao Paulo Medical School Ethical Committee.

Echocardiographic analysis

All studies were performed using the iE33 (Philips Medical Systems, Andover, MA, USA) with transthoracic S3 and X3 broadband transducers (frequency= 2 – 5 MHz).

Two-dimensional echocardiogram

LV volumes and ejection fraction were assessed by two-dimensional echocardiography (2DE) through apical 4- and 2-chamber (A4C, A2C) views, using the modified Simpson's rule, as recommended[5]; data were indexed for body surface in both groups. Images to analyze the LV longitudinal strain were obtained through A4C view at high frame rates (50 to 70 Hz), during apnea, usually with forced expiration.

Pulsed Wave Doppler

The mitral flow velocity was measured by pulsed wave Doppler obtained in A4C view, with the sample volume positioned at the tips of the mitral valve leaflets. Peak early diastolic velocity - E wave, peak late diastolic velocity – A wave, E/A ratio and E wave deceleration time were calculated. The deceleration time (DT) was measured in an interval between the peak E wave and the point where the deceleration curve reaches the baseline. LV myocardial performance index (MPI) was obtained through the mitral diastolic flow, by measuring the time between the closure of the valve and its opening in the next cycle (A time) divided by the ejection time (B time), according to the following formula[6]:

$$MPI = \frac{A - B}{B}$$

Continuous wave and color Doppler

Mitral regurgitation was diagnosed and quantitatively graded by color Doppler, with additional analysis of positive dP/dt as a measure of ventricular systolic function, calculated by continuous wave Doppler, according to the literature[7]. Tricuspid regurgitation (TR) was identified and qualitatively graded by color Doppler; the TR curve obtained by continuous wave Doppler and the estimated right atrial pressure were used to quantitatively estimate the pulmonary systolic arterial pressure, as previously described[8].

Tissue Doppler Imaging (TDI)

The longitudinal myocardial function was assessed by means of myocardial velocities obtained by TDI in the A4C view, with the sample volume positioned on the mitral valve annulus at the septal and lateral walls. Peak systolic velocity (S wave), e' (corresponding to the early diastolic filling) and a' (corresponding to the atrial systole) were determined. The values obtained were used to calculate the eas index (easi), proposed by Mogelvang et al.[9] to express both the systolic and diastolic performance of the LV, according to the formula:

$$easi = \frac{e'}{S \times a'}$$

Normal values ≤ 0.18; higher values indicate worse ventricular performance.

The noninvasive assessment of pulmonary capillary wedge pressure, E / e ' ratio, was calculated after conventional Doppler and TDI. Values > 15 indicate pulmonary capillary pressure > 20 mmHg[10].

Real-time three-dimensional echocardiography (RT3DE)

This technique is more accurate to determine the LV volumes and ejection fraction[11]. The full volume was obtained through the three orthogonal planes: sagittal (corresponding to the long axis), coronal (similar to the apical 4-chamber view) and transversal (corresponding to the short axis). Then, three points were manually plotted: one related to the LV apex and the other two for the mitral valve annulus; after a few seconds, dedicated software (QLAB 7.0, Philips Medical Systems - Andover, MA, USA) automatically detected the endocardial borders and calculated the LV volumes and EF[12].

Longitudinal transmural global strain (GS)

Apical 4C view was used to determine GS by manually positioning three reference points: one on each side of the mitral valve annulus and the third at the apical endocardial border. Immediately, dedicated software (QLAB 8.1, Philips Medical Systems - Andover, MA, USA) creates a region of interest (template) with the automatic delineation of endocardial and epicardial borders, tracking the speckles throughout the cardiac cycle, thus deriving the transmural global strain (Figure 1).

Statistical analysis

Comparisons between the control group and the DCM group were made using the Student's *t* test. If the criteria of normality fail, nonparametric Mann-Whitney test was used. Correlation analysis was performed using Pearson's coefficient and the proportions between the genders were analyzed by chi-square test. P values < 0.05 were considered statistically significant. To test the intra-observer variability, GS analysis was repeated in 15 randomly chosen patients by the same observer in a minimal interval of one month. This variability was expressed as a percent error for each measurement and was determined as the mean difference between the two measurements. The results were expressed as mean ± SD.

Results

Table 1 shows the clinical characteristics of the studied patients (DCM group). The control group was significantly younger than the DCM group (30 + 53 + 8 years and 12 years respectively; p < 0.001) and also comprised a smaller number of male subjects (control group = 45% of men; DCM group = 72% of men; p = 0.047).

Table 2 shows the data of DCM and control groups obtained by two-dimensional echocardiography.

LV end diastolic and end systolic volumes were higher in patients when compared to controls (p < 0.001), whereas LVEF was significantly lower in the DCM group, when compared with normal subjects (p < 0.001).

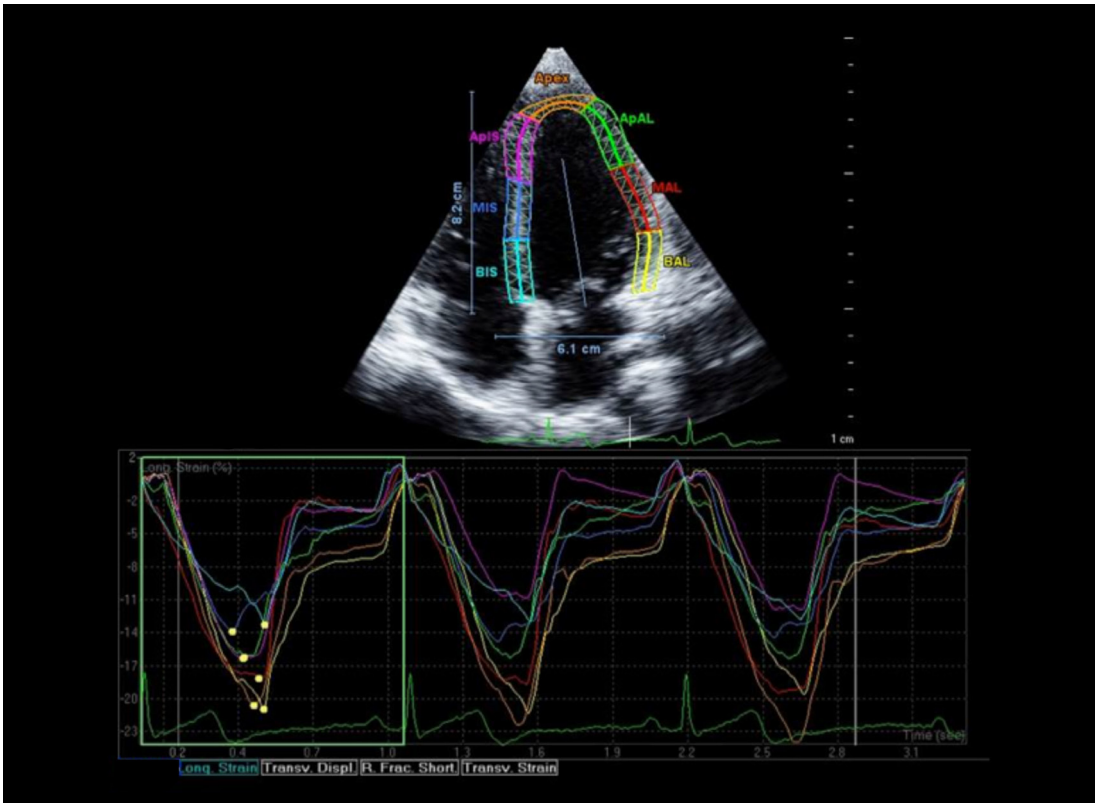

Figure 1 – *Analysis of LV longitudinal myocardial strain by the apical four-chamber view in a normal volunteer. Top: template originated by dedicated software after the points defined by the operator. Bottom: the curves of deformation, colored according to the corresponding segment depicted in the template; the points at the nadir of each curve correspond to peak systolic strain.*

Considering the parameters of diastolic function analysis obtained by pulsed wave Doppler, the peak early diastolic velocity (E) was the only one significantly lower in DCM group, when compared with the controls ($p = 0.021$).

The systolic, early diastolic and late diastolic velocities obtained by TDI (S, e' and a', respectively) were lower in DCM group compared with controls ($p < 0.001$). Regarding E/e' ratio, the higher values were observed in DCM group ($p < 0.001$).

The myocardial performance index measured by TDI (easi) showed no statistical difference between the two groups ($p = 0.691$). Compared with patients, MPI evaluated by pulsed wave Doppler showed lower values in the control group ($p < 0.001$), likewise the systolic pulmonary arterial pressure ($p < 0.001$). The dP/dt could not be compared between the groups, since the mitral regurgitation diagnosed in normal subjects was discrete, preventing an adequate curve for analysis. However, GS was significantly lower in the DCM group ($p < 0.001$) when compared with controls (Figure 2).

In DCM group, the correlation between conventional echocardiographic parameters of ventricular systolic function and GS was positive for the ventricular volumes obtained by RT3DE and negative for the LVEF and S (Figure 3).

Multivariate analysis showed that the only negative predictor of GS in DCM group was the ejection fraction calculated by RT3DE ($R^2 = -0.404 \pm 0.186$, $p = 0.038$), i.e., the smaller the LVEF, the higher the values of GS (indicating lower deformation). There was no correlation between GS and LV volumes, LVEF by 2DE, S velocity, E/e´ratio, MPI, dP/dt and eas index.

The reproducibility of longitudinal transmural global strain assessed by intra-observer variability was 7 ± 0.22.

Discussion

The present study showed that LV deformation in the longitudinal plane estimated by speckle tracking is significantly reduced in patients with severe DCM, when compared with normal individuals. It also showed correlation with conventional echocardiographic parameters, such as ventricular volumes, ejection fraction and S' velocity. LVEF estimated by RT3DE was the only predictor of GS in DCM group.

One of the most important determinants of poor prognosis in DCM is the ventricular remodeling that occurs due to the

Table 1 – Clinical characteristics of patients with dilated cardiomyopathy (DCM group)

Clinical Characteristics	n = 71
Hypertension	42
Dyslipidemia	27
Diabetes mellitus	25
Chagas Disease	25
Familial History	24
Alcohol Abuse	22
Idiopathic	15
Left branch-bundle block	40
PM	10
Beta-blocker	96
ACEI/ARB	93
Diuretics	91
Digitalis	44
Antiplatelet agents	20
CCB	10
Antiarrhythmic drugs	6
Vasodilator	7
Functional Class (NYHA) I	38
II	42
III	20

Results expressed as N%. ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, CCB = calcium channel blocker; PM = pacemaker, NYHA = New York Heart Association.

decrease in mechanical forces, characterized by dilatation (> 20% of the diastolic or end-systolic volume) and LV contractile dysfunction. It is accepted that low LVEF is closely related to symptoms and prognosis, so that the measurement of this parameter by two-dimensional echocardiography is widely used to assess LV systolic function and to define the therapeutic measures. However, some recent studies showed that, in the clinical setting, the measurement of LVEF has important issues, especially related to the accurate determination of the endocardial borders and the need to presume geometric modeling in order to calculate LV volumes[13-15]. RT3DE overcomes LV foreshortening and geometric assumptions; however, it is not yet routinely applied[15]. Likewise LVEF, another established index to assess left ventricular systolic function is the positive dP/dt, also used as a predictor of mortality in patients with CHF[7].

Through STE it is possible to measure LV rotation, torsion and strain along the cardiac cycle by the recognition of speckles smaller than an ultrasound wavelength, using a sum of absolute difference algorithm. Since it is obtained by 2DE conventional gray scale, STE is angle-independent and is less affected by artifacts, acoustic noise and translation motion, unlike tissue Doppler[2,16-18].

Myocardial strain is comprised by three components: longitudinal, circumferential and radial, disposed in a complex helicoid arrangement, in order to facilitate the ejection and suction of the blood[2,19,20]. It is well established that the longitudinal cardiac fibers located in the subendocardium are the first to be affected by myocardial injury[3], and recent studies using STE are in agreement with these results[21,22]. In patients with cardiac hypertrophy of various etiologies, Sun et al.[23] demonstrated that the longitudinal strain showed the best correlation with LVEF and diastolic function indices. It was also demonstrated that the longitudinal global strain can predict cardiovascular events in patients with CHF[24] and death due to different causes in individuals with heart disease[25].

In the present study, LV myocardial strain was significantly lower in DCM group when compared with normal individuals (-5.53 x -14.02 ± 2.34 ± 1.83, respectively); the patients were older and there was a higher number of men in relation to the healthy volunteers. According to the recent HUNT study, Dalen et al.[26], analyzing 1266 healthy subjects, concluded that the strain decreases with age and is lower in men; these results could raise questions about the association between reduced strain and DCM. However, the values of GS are consistent and correlate with the parameters of systolic function assessment obtained by conventional echocardiography that are well established for this disease (Table 2 and Figure 3)[7,10,13].

The longitudinal transmural global strain correlated with LV volumes and LVEF obtained by RT3DE assessment; moreover, the latter was the only predictor of GS. Considering that RT3DE is more robust than 2DE and the analysis of longitudinal deformation can be obtained quickly, semi-automatically and accurately, this novel technology sheds light on the comprehension of severe DCM. The ability to identify, in this population, those patients who are more prone to cardiovascular events is of paramount importance for the therapeutic optimization and targeting, in an attempt to reduce morbidity and mortality, once this disease represents a public health issue due to the increasing incidence and high cost of treatment.

Concerning the DCM group, the increase in E/e´ratio and MPI, as well as the decrease in the late diastolic filling velocity (a´), indicate the presence of diastolic dysfunction, supporting the hypothesis that systole and diastole are closely related[20].

Limitations

The main limitations of STE are related to the need for image acquisition with higher technical quality (not always possible in the clinical setting) and to the low temporal resolution.

Speckle tracking results from the sum of absolute difference algorithm; thus, the higher the frame rate, the greater the reliability of the results. This may represent an issue when considering patients with ventricular dilatation, since it is often necessary to increase the sector angle in order to allow a complete visualization of the heart. On the other hand, very high temporal resolutions impair the detection of abnormalities because of those speckles with velocities near zero, which can produce mathematical instability in the algorithm[1,16].

Table 2 – Echocardiographic characteristics of the control group and DCM group

Parameter	Control Group	DCM Group	p
N	20	71	
BSA (m^2)	1.74 ± 0.20	1.76 ± 0.17	0.586
Age	30 ± 8	53 ± 12	< 0.001*
Men	45	72	0.047*
HR bpm	72 ± 6	69 ± 13	0.80
2DE LVEDV (ml/m2)	68.06 ± 12.00	125.83 ± 38.44	< 0.001*
2DE LVESV (ml/m2)	25.93 ± 5.08	95.30 ± 32.94	< 0.001*
2DE LVEF%	62.40 ± 2.91	25.37 ± 6.43	< 0.001*
RT3DE LVEDV (ml/m2)	59.64 ± 27.49	129.41 ± 43.08	< 0.001*
RT3DE LVESV (ml/m2)	22.55 ± 10.89	97.48 ± 36.06	< 0.001*
RT3DE LVEF%	62.28 ± 3.99	25.46 ± 6.07	< 0.001*
Absent MR	90	8	---
Discrete MR	10	7	---
Mild MR	---	58	---
Moderate MR	---	14	---
Severe MR	---	7	---
Absent TR	75	37	---
Discrete TR	25	7	---
Mild TR	---	47	---
Moderate TR	---	4	---
Severe TR	---	4	---
E cm/s	88.32 ± 11.41	77.45 ± 24.33	0.021*
A cm/s	55.65 ± 8.07	60.56 ± 29.12	0.615
E/A	1.60 ± 0.17	1.62 ± 1.06	0.230
TD ms	156.45 ± 17.85	198.47 ± 82.56	0.098
s' cm/s	9.58 ± 1.98	4.74 ± 1.02	< 0.001*
e' cm/s	14.42 ± 3.12	6.37 ± 7.25	< 0.001*
a' cm/s	8.21 ± 1.67	5.90 ± 2.09	< 0.001*
easi cm/s	0.19 ± 0.05	0.28 ± 0.35	0.691
E/e'	6.23 ± 1.08	14.61 ± 6.95	< 0.001*
MPI	0.32 ± 0.09	0.86 ± 0.25	< 0.001*
PASP mm Hg	24.00 ± 4.53	44.15 ± 12.4	< 0.001*
dP/dt	---	617 ± 189	---
GS%	-14.02 ± 1.83	-5.53 ± 2.34	< 0.001*

*Data expressed as mean ± SD or n (%). BSA = body surface area, HR = heart rate; 2DE = two-dimensional echocardiography, LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LVEF = left ventricular ejection fraction; RT3DE = real-time three-dimensional echocardiography; MR = mitral regurgitation; TR = tricuspid regurgitation, E = peak early diastolic velocity by pulsed Doppler, A = peak late diastolic velocity by pulsed Doppler; DT = deceleration time; S = peak systolic velocity by tissue Doppler, e '= peak early diastolic velocity by tissue Doppler; a'= peak late diastolic velocity by tissue Doppler; easi = myocardial performance index by Tissue Doppler Imaging; MPI = myocardial performance index by pulsed wave Doppler; PSP = pulmonary artery systolic pressure; GS = longitudinal transmural global strain. * P value with statistical significance (Student's t test)*

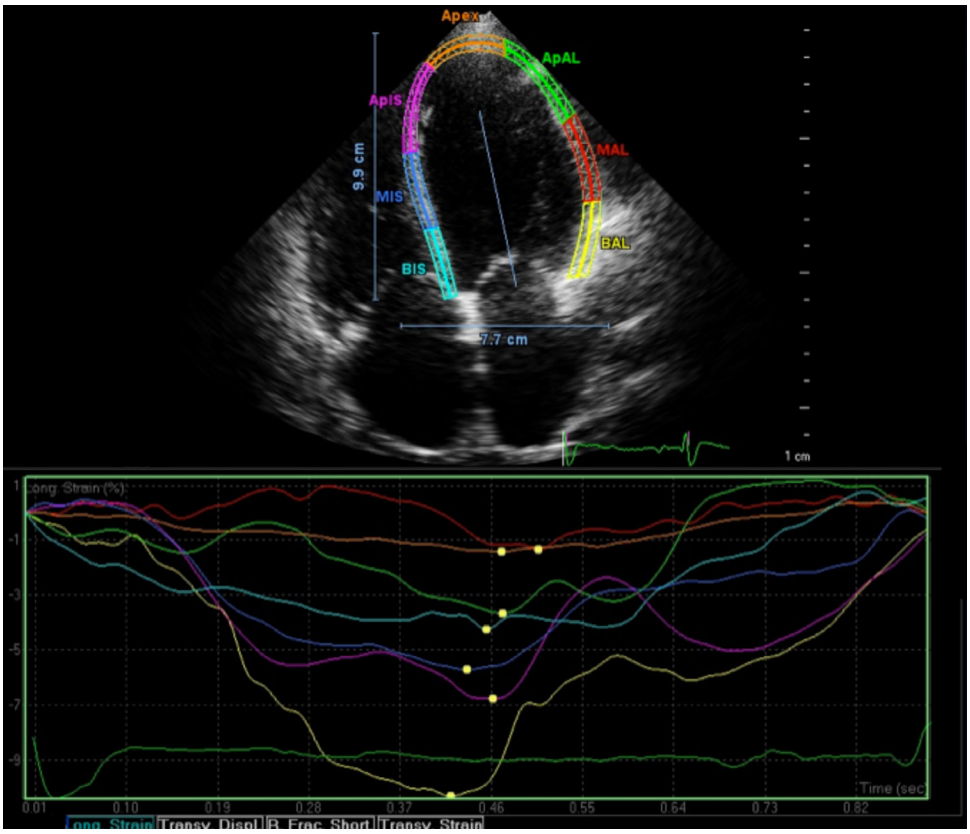

Figure 2 – *Longitudinal myocardial deformation in a patient from DCM group. Observe the decrease in global longitudinal transmural strain (GS = -4.4%).*

Conclusions

The present study demonstrated that longitudinal transmural global strain is significantly reduced in patients with severe DCM; this parameter correlates with ventricular volumes and LVEF obtained from RT3DE. Based on that, new possibilities arise for therapeutic and prognostic evaluation in this specific group of patients.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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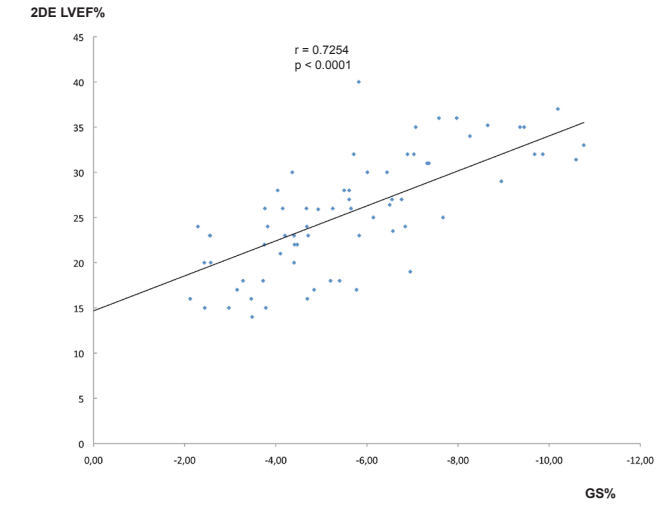

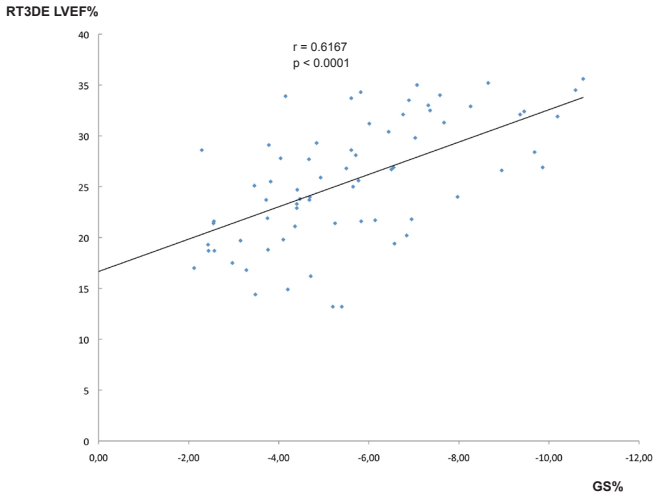

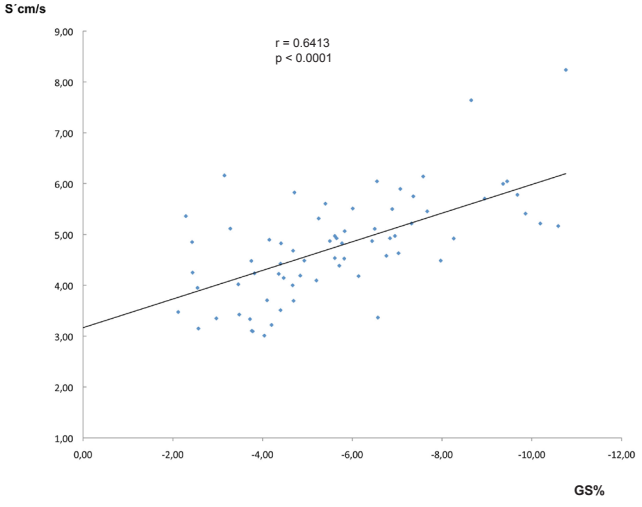

Figure 3 – *Correlation analysis between conventional echocardiographic parameters of systolic function and global strain (GS) in patients with dilated cardiomyopathy. **A**. 2DE LVEF = left ventricular ejection fraction by two-dimensional echocardiography, **B**. RT3DE LVEF = left ventricular ejection fraction by real-time three-dimensional echocardiography; **C**. S'= peak systolic velocity at Tissue Doppler Imaging. Pearson's correlation coefficient.*

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