Original article

Myocardial Deformation (Strain) and Myocardial Fibrosis in Mild Cardiac Chagas Disease

Deformação Miocárdica (Strain) e Fibrose Miocárdica na Forma Cardíaca Leve da Doença de Chagas

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Abstract

Background: The early identification of myocardial damage seems important in the management of patients with Chagas disease. However, it is unknown whether speckle tracking echocardiography strain and cardiac magnetic resonance imaging are promising methods for assessing myocardial involvement and fibrosis, respectively.

Objective: To evaluate myocardial involvement in the mild chronic cardiac form of Chagas disease using speckle tracking strain and myocardial fibrosis by cardiac magnetic resonance and assess their correlations.

Method: This cross-sectional study analyzed patients with the mild chronic cardiac form of Chagas disease (preserved ejection fraction) using speckle tracking echocardiography and cardiac magnetic resonance.

Results: The study included 21 participants (women: 62%; age: 54 ± 5 years). The prevalence of myocardial fibrosis was 50% on delayed myocardial enhancement. The median global longitudinal strain was decreased (14.1%; interquartile range, 12.1–16.3%) in 17 patients (81%). The mean T1 mapping value was high in patients with Chagas disease (993 ± 163 ms). The T1 map was significantly correlated with the global longitudinal strain (r = 0.634; p = 0.015). In addition, the mechanical dispersion index obtained by strain was increased (>55 ms) by 84%, with the largest area under the receiver operating characteristic curve (area under the curve, 0.696; 95% confidence interval, 0.412–0.981) for fibrosis discrimination by delayed myocardial enhancement.

Conclusion: Myocardial strain and T1 mapping are early markers of myocardial damage in mild chronic Chagas heart disease. The mechanical dispersion index was high and the most closely correlated with delayed myocardial enhancement.

Keywords: Cardiac magnetic resonance; Chagas disease; Myocardial fibrosis; Myocardial strain; Speckle tracking echocardiography.

Resumo

Fundamento: A identificação precoce do dano miocárdico parece ser importante na abordagem do paciente com doença de Chagas. A ecocardiografia com *strain* obtida por *speckle tracking* e a avaliação da fibrose miocárdica por meio da ressonância magnética cardíaca podem ser métodos diagnósticos promissores nesse sentido.

Objetivo: Avaliar o acometimento miocárdico especificamente na forma crônica cardíaca leve da doença de Chagas por meio do *strain* por *speckle tracking* e da fibrose miocárdica pela ressonância magnética cardíaca, além de suas correlações.

Método: Estudo de corte transversal que analisou portadores da forma cardíaca crônica leve da doença de Chagas (fração de ejeção preservada) submetidos à ecocardiografia com *strain* por *speckle tracking* e à ressonância magnética cardíaca.

Resultados: Foram incluídos 21 participantes (mulheres: 62%; idade: 54 ± 5 anos). A prevalência de fibrose miocárdica por meio do realce tardio miocárdico foi de 50%. O *strain* longitudinal global encontrava-se diminuído em 17 pacientes (81%), com mediana de 14,1% (intervalo interquartil de 12,1 a 16,3). Os valores do mapa T1 encontravam-se, em média, elevados nos portadores de doença de Chagas (993 ± 163 ms). O mapa T1 foi significativamente correlacionado com o *strain* longitudinal global (r= 0,634; p = 0,015). Além disso, o índice de dispersão mecânica, obtido por *strain*, estava aumentado (> 55 ms) em 84%, com a maior área sob a curva Característica de Operação do Receptor (área sob a curva de 0,696; intervalo de confiança de 95% de 0,412-0,981) para discriminação de fibrose pelo realce tardio miocárdico.

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Manuscript received 12/14/2020; revised 2/19/2021; accepted 3/30/2021

DOI: 10.47593/2675-312X/20213403eabc173

Conclusão: O *strain* miocárdico e o mapa T1 se comportam como marcadores precoces do dano miocárdico na cardiopatia chagásica crônica leve. O índice de dispersão mecânica estava elevado e foi o parâmetro que melhor se correlacionou com o realce tardio miocárdico.

Palavras-chave: Doença de Chagas; Ecocardiografia *speckle tracking*; *Strain* miocárdico; Ressonância magnética cardíaca; Fibrose miocárdica.

Introduction

chagas disease (CD), an infection caused by the parasite *Trypanosoma cruzi*, affects 6– 7 million people worldwide and leads to 10,000 deaths annually.[1] An estimated 20–40% of infected people will develop the cardiac form of CD, although it is not possible to identify which patients will develop chronic Chagas cardiomyopathy.[2,3] The early identification of myocardial damage seems important in individualizing the management of patients with CD.

Previous studies using conventional transthoracic echocardiography (TTE) showed early cardiac involvement in CD patients without ventricular dysfunction from the indeterminate form.[4-8] Regional contractility changes, including aneurysms, were observed on TTE in 54% of CD patients without ventricular dilatation or heart failure.[6]

Speckle tracking echocardiography (STE) has recently been used to evaluate myocardial deformation (strain). This method, validated in relation to cardiac magnetic resonance (CMR) and sonomicrometry, requires no contrast, has little inter- and intraobserver variability, and is angle-independent.[9-12] The strain evaluated by STE is considered a sensitive and specific indicator of subclinical ventricular dysfunction.

Myocardial fibrosis (MF) determined by CMR imaging, which uses delayed gadolinium enhancement and T1 mapping, has been considered an important prognostic marker in several cardiac pathologies. In the cardiac form of CD, CMR allows the early identification of cardiac involvement and more precise stratification of cardiomyopathy severity.[13-16]

This study aimed to evaluate myocardial involvement in the mild chronic cardiac form of CD using STE strain and the MF using CMR and determine their correlations.

Methods

This analytical cross-sectional study was performed from October 2014 to July 2015. The study population was 25 patients with the mild chronic cardiac form of CD determined by electrocardiographic changes (conduction disorders and/or arrhythmias) and a left ventricular ejection fraction (LVEF) ≥ 50% who were followed up in a specialized clinic. The participants belonged to the B1 group of cardiac involvement according to international recommendations adapted to Chagas etiology.[3,13] The research subjects were consecutively invited to participate in this study.

The inclusion criteria were mild chronic cardiac CD confirmed by two serological tests (indirect hemagglutination and indirect immunofluorescence) and age 18–65 years. The exclusion criteria were as follows: inappropriate acoustic window for TTE or more than two left ventricular (LV) segments not analyzed by STE; previous diagnosis of cardiomyopathy of another etiology; coronary artery disease; previous treatment with benznidazole; cardiac arrhythmia, diabetes mellitus, systemic arterial hypertension, or infectious or chronic degenerative diseases; and use of immunosuppressive or hepatotoxic drugs. All participants underwent a structured medical history analysis, physical examination, electrocardiography, chest radiology, two-dimensional Doppler echocardiography, and STE.

The study was approved by the Research Ethics Committee of the Bahiana School of Medicine and Public Health, and each participant signed an informed consent form.

Speckle Tracking Echocardiography

The participants underwent echocardiography using a commercially available ultrasound system (iE33, Philips Medical Systems, Andover, MA, USA) equipped with a 2.5–4 MHz transducer. Images were taken by an investigator and reviewed offline by two experienced echocardiographic observers. Three cines of cardiac cycles were digitally recorded and stored for subsequent analysis. Chamber dimensions and thicknesses were obtained according to American Society of Echocardiography (ASE) recommendations.[17]

Two-dimensional images were obtained at a cycle frequency of 50–70 cycles per second using tissue harmonic imaging and a high-quality electrocardiogram signal. The images were evaluated on a workstation equipped with QLab software (Philips Medical Systems). STE was used to assess myocardial deformation. All images were analyzed using the model proposed by the American Heart Association/American College of Cardiology with 16 segments.[18] Apical four-, three-, and two-chamber views were used to measure the global longitudinal strain (GLS) and the mechanical dispersion index (MDI), also obtained by longitudinal strain, which refers to the standard deviation of time for maximum deformation of the 16 segments. Mid-ventricular short-axis images were used to assess circumferential (SCi) and radial (SR) strain.

The normal percentage of peak longitudinal systolic strain (LS) varies among software references. The Phillips QLab reference value is 18.9% ± 2.5%. The lower limit of normal is 14%. The SCi and SR reference values were 22.1% ± 3.4% and 35.1% ± 11.8%, respectively. As suggested, the absolute numerical value without the negative or positive sign was used when referring to LS, SCi, or SR.[10] An MDI greater than 55 ms is considered high.[19,20]

Cardiac Magnetic Resonance

CMR was performed on an Avanto 1.5 T full-body scanner (Siemens Medical Solutions, Germany) using an eight-channel cardiac coil array. Cine images were acquired using a proton-free processing sequence synchronized with heart rate during apnea (acquisition rate, 20 frames/cardiac cycle; slice thickness, 8 mm; field of view, 300; matrix,

208; Åx, 80; bandwidth, 925 KHz/pixel). LV function was analyzed using eight and 12 8-mm-thick and 2-mm apart short-axis slices. Ventricular volume, mass, and systolic function, including right ventricle and LV ejection fraction, were calculated using CMR cine images and Argus 4D VF software. Endocardial contours were manually drawn during systole and diastole.

Multi-axis acquisition of cardiac prototypes was performed using the T1 MOLLI sequence for individual short-axis slices. Automated T1 maps were generated for manual calculation using analysis of the region of interest.

Fibrosis was analyzed using delayed myocardial enhancement (DME) after the intravenous infusion of 0.2 mmol/kg of gadolinium-tetraazacyclododecane tetraacetic acid (Dotarem® [gadoteric acid]; Gerbet Produtos Médicos, Rio de Janeiro, Brazil). DME images were taken in short-axis view with 8-mm thickness from the LV base to the apex at 5–15 minutes after the gadolinium administration using the following parameters: repetition time, two RR intervals; excitation time, 4–4.8 ms; 256 × 192 matrix image; field of view, 300–400 mm; spacing, 2.0 mm; deflection angle, 30°; and inversion time, adjusted on a case-by-case basis to nullify the normal myocardial signal.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation or median and interquartile range (IQR; 25%–75%) depending on normality on the Shapiro-Wilk test. Categorical variables are expressed as total number (percentage). Student's t-test was used to examine normally distributed numerical variables, while the Mann-Whitney nonparametric test was used to examine non-normally distributed variables. Pearson's correlation coefficient was used to assess the association between GLS and TTE and T1 mapping parameters. Binary logistic regression was used to test the independent association between strain and CMR variables. Receiver operating characteristic (ROC) curves were constructed to identify the best strain and T1 mapping cutoff points to predict fibrosis. Considering the study's exploratory nature, sample size was not measured. Based on a published article,[15] we included 25 participants. The analyses were performed using SPSS software version 21.0 (IBM), and p values <0.05 were considered statistically significant (test).

Results

Clinical Characteristics and Echocardiographic Data

Three (13%) research subjects were excluded from the analysis for poor echocardiographic image quality, while another was excluded due to cardiac arrhythmia. Thus, the final study population was 21 participants. Women accounted for 62% of the patients, and the mean patient age was 54 ± 5 years.

Six (29%) participants had a significant segmental change, including four (19%) with apical LV aneurysms, one (5%) with a basal septal aneurysm, and one (5%) with basal hypokinesia in the inferior lateral wall. The patients' clinical characteristics and echocardiographic data are shown in Table 1.

Table 1 - Patients' clinical and epidemiological characteristics.

Characteristics	(n = 21)
Age, years	54 ± 5
Female sex	13 (62)
NYHA classification > I	3 (14)
HR, bpm	69 ± 9
SBP, mmHg	126 ± 12
DBP, mmHg	77 ± 11
Radiological aspects	
Increased CTI	5 (24)
ECG aspects	
Isolated RBB	7 (33)
Isolated ASDB	4 (19)
RBB + ASDB	10 (48)
Simpson's LVEF, %	63 ± 6
LVEDD, mm	49 ± 3
LVESD, mm	31 ± 3
LV mass/m^2 g/m^2	83 ± 15
LVDVi, mL/m^2	67 ± 12
LVSVi, mL/m^2	18 ± 6
LAVi, mL/m^2	27 ± 8
LV diastolic dysfunction	
Grade I	13 (62)
Grade II	2 (9)
Segmental change	6 (29)
Apical aneurysm	4 (19)

Results are expressed as mean ± standard deviation or n (%). ASDB, anterior superior divisional block; CTI, cardiothoracic index; DBP, diastolic blood pressure; ECG, electrocardiogram; HR, heart rate; LAVi, left atrial volume index; LV, left ventricle; LVDVi, left ventricular diastolic volume index; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVSVi, left ventricular systolic volume index; NYHA, New York Heart Association; RBB, right bundle branch block; SBP, systolic blood pressure.

GLS and MDI by Speckle Tracking

The GLS was reduced in 81% of the samples (median, 14.1%; IQR, 12.1–16.3). Of them, 10 (48%) participants already had a frankly abnormal GLS decrease (< 14%). Table 2 shows the LS values.

The apical and middle portions of the LV were the most involved (62% and 57%, respectively), while only 38% of the basal portion had a GLS with a frankly abnormal decrease.

The myocardial performance index presented a mean of 88.6 ms and a median of 83.4 ms (IQR, 58.6–108.6 ms).

Correlation between GLS and Conventional Echocardiography Findings

The GLS was significantly correlated with LVEF (r = -0.512; p = 0.018) and the S' value (r = - 0.511; p = 0.018). GLS differed significantly between groups with and those without segmental changes (12% ± 1.2% versus 14.5% ± 2.8%, p = 0.049).

SCi and SR in Cardiac CD

The patients' SCi and SR myocardial deformations at the mid-ventricular level are shown in Table 3. The mean SR was significantly reduced in 13 patients (65%), while the mean SCi was significantly reduced in 11 patients (55%).

MF by CMR

Sixteen participants underwent CMR. The prevalence of MF by DME in the sample was 50%. The patients were divided into two groups according to the presence or absence of MF. The clinical characteristics did not differ significantly between the groups. The patients' clinical and echocardiographic characteristics (Table 4) did not differ significantly between groups.

The prevalence of segmental contractility changes detected on TTE was higher in the MF group (37.5% versus 12.5%). The two cases of grade II diastolic dysfunction were also in the MF group.

Strain values in the different orthogonal, longitudinal, circumferential, and radial axes did not differ by the presence of MF by DME. The median 16-segment MDI obtained by strain was higher in the MF group (90.7 m; IQR, 72–121 ms) than in the group without MF (67 ms; IQR, 53.5–109 ms), but the difference was not statistically significant (p = 0.23).

Table 2 – Left ventricular global and segmental longitudinal strain.

	n = 21
Global	14.1 (12.1; 16.3)
Anterior	18.4 (14.9-22.5)
Anterior septal	15.4 (10.8-17.2)
Inferosseptal	12.4 (-7.1-17.0)
Basal	
Inferior	16.9 (12.3-19.5)
Inferior lateral	17.2 (12.8-23.5)
Anterior lateral	20.2 (-8.9-25.4)
Mean value	16.2 (12.2-19.4)
Anterior	11.4 (9.9-15.8)
Anterior septal	13.8 (9.1-19.0)
Inferior septal	14.2 (10.1-17.9)
Middle	
Inferior	14.9 (11.6-17.7)
Inferior lateral	14.8 (9.4-16.7)
Anterior lateral	10.6 (8.6-15.2)
Mean value	12.9 (11.5-15.7)
Anterior	9.1 (5.8-12.5)
Septal	13.7 (11.2-18.0)
Apical	
Inferior	19.5 (15.7-22.5)
Lateral	11.7 (7.4-14.6)
Mean value	13.4 (11.0-16.2)

Results are expressed as median and interquartile range (25%-75%). Strain data are expressed as percentages.

Table 3 - Circumferential and radial strains of the middle portion of the left ventricle.

Global (middle)	Circumferential strain n = 20 15.2 (12.4-17.1)	Radial strain n = 20 17.6 (12.3-24.1)
Anterior	12.7 (7.9-16.8)	17.8 (12.2-29.5)
Anterior septal	14.8 (10.4-23.3)	14.9 (7.4-22.2)
Inferior septal	15.0 (12.2-21.5)	15.4 (10.5-31.0)
Inferior	14.2 (10.7-16.6)	19.6 (12.3-30.3)
Inferior lateral	14.1 (9.7-16.7)	20.6 (14.7-25.5)
Anterior lateral	13.9 (9.6-17.6)	16.1 (11.8-30.3)

Results are expressed as median and interquartile range (25%-75%). Strain data are expressed as percentages.

Table 4 - Clinical and echocardiographic data by presence of myocardial fibrosis by delayed enhancement on cardiac magnetic resonance.

Variable	Presence of MF (n = 8)	Group MF (n = 8)	P value
Age, years	54.8 ± 6.4	53.4 ± 3.6	0.382
Female sex	3 (37.5)	8 (100)	0.009
Previous stroke	1 (12.5)	0	0.317
HR, bpm	66.8 ± 9.5	73.1 ± 6.8	0.146
SBP, mmHg	126.3±10.6	121.9± 11.9	0.451
DBP, mmHg	76.3 ± 11.9	76.9 ± 13.3	0.923
BMI, kg/m^2	27.3 ± 4.2	27.1 ± 4.9	0.941
NYHA > I	1 (12.5)	0	0.317
LVEDD, mm	48 ± 3.7	48 ± 3.7	0.682
LVESD, mm	32 ± 4.3	29 ± 2.8	0.178
LV indexed mass, g/m^2	90 ± 17	77 ± 9.8	0.328
LVDVi, mL/m^2	66 ± 16	64 ± 12	0.770
LVSVi, mL/m^2	20 ± 8	15 ± 4.3	0.442
LAV/m2, mL/m^2	31 ± 10	27 ± 7.8	0.367
LVEF, %	64 ± 7.4	65 ± 5.6	0.630
E wave, cm/s	69 ± 14	75 ± 23	0.798
A wave, cm/s	80 ± 12	80 ± 21	0.878
E/A ratio	0.9 ± 0.2	1.0 ± 0.4	0.498
Mean e', cm/s	7.3 ± 2.7	8.0 ± 2.1	0.474
Mean S', cm/s	7.4 ± 0.9	7.6 ± 1.2	0.690
E/e' ratio	9.8 ± 3.1	9.4 ± 2.1	0.750
GLS, %	14.3 (11.9-18.6)	14.4 (12.3-16.3)	0.681
Mean SR, %	20.0 (16.8-23.8)	18.0 (12.3-26.2)	0.694
Mean SCi, %	13.9 (10.5-17.5)	15.8 (14.6-17)	0.536
MDI, ms	90.7 (72-121)	67 (53.5-109)	0.233
MDI > 85, ms	6 (75.0)	2 (25.0)	0.067

Results are expressed as mean ± standard deviation, n (%), or median (25-75% interquartile range). Strain data are expressed as percentages. Student's t-test was used to examine normally distributed variables. The Mann-Whitney test was used to examine non-normally distributed variables. Fisher's exact test was used to examine categorical variables. BMI, body mass index; DBP, diastolic blood pressure; GLS, global longitudinal strain; HR, heart rate; LAV, left atrial volume; LV, left ventricle; LVDVi, left ventricular end-diastolic volume index; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVSVi, left ventricular end-systolic volume index; MDI, mechanical dispersion index; NYHA, New York Heart Association; SBP, systolic blood pressure; SCi, circumferential strain; SR, radial strain.

ROC curves were constructed to analyze the discrimination capacity of GLS for the presence of MF using delayed gadolinium enhancement. The GLS presented a C-statistic (AUC) of 0.516 (95% confidence interval [CI], 0.215–0.816). The best GLS cutoff point was 13.97%, with a sensitivity of 62.5% and specificity of 50%. MDI had the highest AUC (0.696; 95% CI, 0.412–0.981) (Figure 1). The best MDI cutoff point was 85 ms, with a sensitivity of 75% and specificity of 71%. Six of the eight patients (75%) with MF had an MDI > 85 ms, while only two (25%) without MF had an MDI > 85 ms, and the difference was of borderline statistical significance (p = 0.067) (Table 7).

T1 mapping with native T1-weighted early global enhancement sequence was also used to assess MF. T1 mapping values were high in patients with CD (mean, 993 ± 163 ms). The median T1 mapping values were 1,033 for the group with MF (IQR, 998–1.081), and 1,010 for the group without MF (IQR, 1,002–1,047). The times were even higher in the MF group, corroborating the finding in cases of other dilated cardiomyopathies. According to the ROC curve analysis, the best T1 mapping cutoff point for identifying MF was > 1,013.6, with a sensitivity of 71%, specificity of 57%, and AUC of 0.592 (Figure 1).

In the simple linear regression analysis, T1 mapping value was significantly correlated with GLS (r = -0.634; p = 0.015). A GLS < 13% had 83% sensitivity and 50% specificity for identifying a T1 mapping value > 1,013.6.

Discussion

In this study, myocardial strain obtained by STE, T1 mapping, and DME obtained by CMR functioned as markers of early cardiac involvement in patients with chronic cardiac CD. These findings suggest the presence of subclinical systolic dysfunction in this population.

Myocardial strain proved to be a sensitive method for identifying early ventricular contractility abnormalities. The data of this study corroborate evidence reported in other studies.[13,21-24] The mean global strain was decreased in all orthogonal axes (longitudinal, radial, and circumferential) in patients with chronic cardiac CD without ventricular dysfunction, with predominant changes seen in the apical segments, confirming the segmental nature of Chagas cardiomyopathy and its predilection for affecting the apical region of the LV, but other segments were also affected.

The literature has also demonstrated this segmental involvement variability, especially in the radial and circumferential assessment of the strain obtained by STE.[21] Using only conventional two-dimensional echocardiography, the apical, inferior basal, basal inferolateral, and basal septal segments are the most commonly affected by this pathology.[6]

Most studies of myocardial deformation in CD, unlike this study, evaluated patients with the indeterminate form or CD without cardiac involvement.[21-23] Barbosa et al.[23] reported that SR involvement occurs the earliest in Chagas cardiomyopathy and suggested that this SR change is due to the mid-myocardial involvement of fibrosis in chronic CD without heart disease.

Patients with the chronic cardiac form of CD and a preserved ejection fraction, in addition to presenting decreased segmental and GLS presented a significantly reduced myocardial SCi and global SR at the mid-ventricular level.

An original finding of this study is our evaluation of mechanical dispersion in this phase of CD, which revealed an increased MDI (>55 ms) in 84% of patients.

Table 5 - Univariate linear regression analysis of dependent variable T1 mapping time by cardiac magnetic resonance.

Variable	Beta	P value
GLS,%	-0.634	0.015
Mean SCi, %	0.412	0.143
Mean SR, %	-0.260	0.370
MDI, ms	-0.198	0.516

GLS, global longitudinal strain; MDI, mechanical dispersion index; MR, radial strain; SCi, circumferential strain.

Table 6 - Mechanical dispersion index and delayed gadolinium enhancement.

Dispersion index (ms)	Delayed enhancement		Total	P value
	No	Yes		
≤ 85	5	2	7	
> 85	2	6	8	0.067
Total	7	8	15	

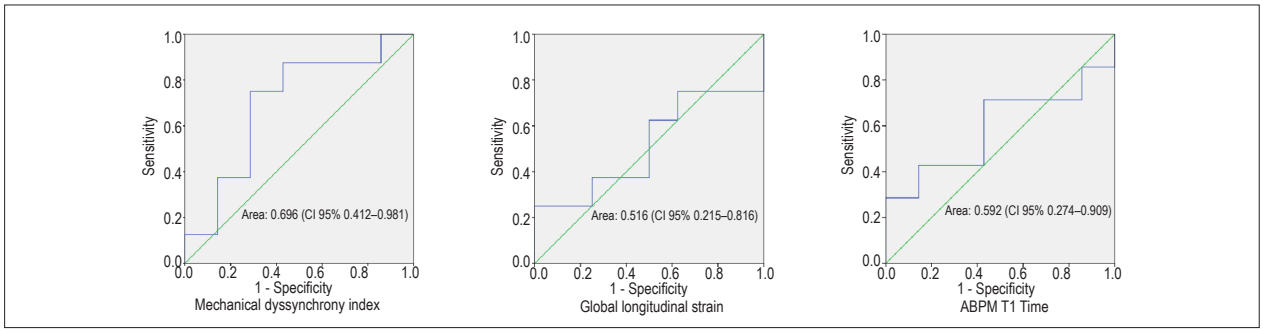

Figure 1 – *ROC curves to determine the presence of late gadolinium enhancement using mechanical dyssynchrony index, global longitudinal strain and ABPM T1 time. Greater area under the curve for the mechanical dyssynchrony index.*

In the analysis using CMR, only half of our patients had MF by DME. As reported in a previous study,[25] there was no statistically significant correlation between MF by DME and GLS, SCi, and SR, probably because the strain is already changed in patients without fibrosis identified by DME or due to the small number of patients (n = 16) undergoing CMR. However, using T1 mapping, which detects myocardial changes more comprehensively and sooner than DME, a statistically significant correlation was observed with GLS, reinforcing the idea that the strain changes very early. The parameter that best correlated with MF by DME was the MDI, with a higher AUC-ROC curve for MDI (0.696) than for GLS (0.516). An MDI > 85 ms had a sensitivity of 75% and a specificity of 71% for predicting MF by DME. This finding has not yet been described in patients with the chronic mild cardiac form of CD.

The prognostic role of strain in CD remains unclear. Current findings indicate the need for prospective longitudinal studies using strain, and the present data suggest that the addition of MDI as a relevant parameter to T1 mapping and DME can help identify patients at higher risk of developing more severe myocardial dysfunction in the future.

Conclusion

Abnormal myocardial speckle tracking strain occurs very frequently in chronic Chagas heart disease with preserved ejection fraction. Strain values in the different orthogonal axes showed no difference by the presence of MF using the DME technique. T1 mapping by CMR was significantly correlated with GLS and seemed to identify myocardial changes earlier than DME in Chagas heart disease. Our findings show that MDE using strain can improve the discriminatory power of the presence of MF.

Due to its cross-sectional design, this study was not able to establish a precise relationship between MF and myocardial strain. The small sample size is due to the difficulty identifying patients with subclinical forms of CD seeking health services. Despite the standardization of the protocol for offline echocardiogram analysis, intra- and interobserver variability were not analyzed. Thus, it was not possible to quantify MF using the DME technique, nor was it possible to perform CMR in all participants due to service unavailability.

Authors' Contributions

Conflict of interest

The authors have declared that they have no conflict of interest.

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