Original Article

The Value of Two-dimensional Strain in the Diagnosis of Acute Myocarditis: Comparison with Cardiac Magnetic Resonance Imaging

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Abstract

Introduction: Acute myocarditis is a major cause of sudden death in young patients. Cardiac magnetic resonance imaging (CMR) is a sensitive noninvasive method to detect myocarditis, but it is costly and unavailable in most medical centers. Two-dimensional strain is a new echocardiographic technique that evaluates myocardial strain to analyze global and regional myocardial function.

Objetive: To assess the value of two-dimensional strain in patients diagnosed with myocarditis.

Material and methods: We prospectively studied patients with acute myocarditis and normal cardiac contractility using CMR, who underwent conventional echocardiography and two-dimensional strain. The ventricular myocardium was divided into 16 segments and these segments were divided into two groups. Group 0: normal myocardial segment by CMR. Group 1: myocardial segment compatible with myocarditis using CMR.

Results: The study evaluated 28 patients, including 82,1% (n = 46) males with a mean age of 35.6 ± 8.9 years. Of the 448 myocardial segments evaluated, 316 segments were normal (group 0) and 132 segments (group 1) were diagnosed with myocarditis using the late enhancement technique on CMR. The analysis of two-dimensional strain showed a significant difference between the groups (19.6 ± 2.9 versus 15.4 ± 2.8 p = 0.001), with 75% sensitivity and 79% specificity and AUC of 0.86 (95% CI 0.82 to 0.89).

Conclusion: Two-dimensional strain can be useful in the evaluation of patients with myocarditis, normal contractility by CMR and conventional echocardiography. (Arq Bras Cardiol: Imagem cardiovasc. 2017;30(1):3-7)

Keywords: Myocarditis; Magnetic Resonance Spectroscopy/methods; Echocardiography/methods.

Introduction

Myocarditis is a major cause of sudden death in individuals younger than 40.[1] This rate may be underestimated due to diagnostic difficulties, but the reports of autopsy studies estimate an incidence between 0.2 and 12% depending on the population studied.[2]

Cardiac magnetic resonance imaging (CMR) is the method of choice in the diagnosis of acute myocarditis.[3] The three main CMR techniques used in the characterization of myocardial injury are T2-weighted sequences, global early myocardial enhancement and delayed enhancement. The presence of abnormalities in at least one of the techniques mentioned above shows 67% sensitivity, 91% specificity and 78% accuracy.[3] However, this method is costly and accessible only in large diagnostic centers, restricting its use in everyday clinical practice.

Conventional echocardiography presents limitations for diagnosing myocarditis. Among the new echocardiographic techniques developed recently, the two-dimensional strain is an accessible low-cost option (software available in all medium and large-size devices, including portable devices) with high accuracy and reproducibility. This method delivers real-time evaluation of the quantitative indices of intrinsic cardiac strain, providing an accurate assessment of regional contractility. However, it remains unclear whether this new technique has any additional usefulness over CMR and conventional echocardiography for the diagnosis of acute myocarditis.[4]

The objective of this study was to evaluate the value of two-dimensional strain in patients with acute myocarditis using CMR, with normal contractility on CMR and conventional echocardiography.

Material and Methods

From January 2012 to December 2015, we evaluated patients with myocarditis, with normal contractility on CMR, who underwent conventional echocardiography and two-

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dimensional strain using the speckle tracking technique. Patients were selected according to the following criteria: a clinical picture suggesting acute coronary syndrome (chest pain, positive troponin and/or abnormalities on electrocardiography), normal coronary angiography and CMR with diagnosis suggesting myocarditis. Exclusion criteria were: Inability or no availability to do the tests proposed; history of acute myocardial infarction (AMI); complete left bundle branch block; presence of pacemaker; presence of severe valve disease; atrial fibrillation; any other severe chronic or acute cardiac or systemic disease, which could affect the results of specific tests; pregnancy.

Ventricular myocardium was divided into 16 segments by CMR and two-dimensional strain and these segments were divided into two groups. Group 0: normal myocardial segment by CMR. Group 1: myocardial segment compatible with myocarditis on CMR.

This study was approved by the Research Ethics Committee (CEP) of Faculdade da Saúde e Ecologia Humana (Faseh) with Certificate of Presentation of Ethics Appreciation (CAAE) number 42744715.5.0000.5101.

Cardiac magnetic resonance imaging

CMR was performed on a 1.5 Tesla equipment (Magnetom; Siemens Medical Systems, Rotterdam, The Netherlands). Specific sequences were acquired for the evaluation of ventricular function, myocardial perfusion at rest and evaluation of myocarditis (T2-weighted sequences, early myocardial enhancement and delayed enhancement).[3] The myocardial segments were evaluated in 16 segments, according to the echocardiography. Assessment and calculation of LV measurements were performed on a workstation dedicated to cardiology tests on CMR through specific software.

Echocardiography and two-dimensional strain

All patients were referred to transthoracic echocardiography 24 hours after admission, including two-dimensional longitudinal strain using speckle tracking. The tests were performed on an echocardiography device Vivid E9 (General Electric, Milwalkee, WI, USA). Images were taken on apical 4 and 2 chamber sections and longitudinal apical sections, properly synchronized with echocardiography and stored for further analysis with appropriate software (EchoPAC, GE Healthcare Technologies Ultrasound). Sixteen myocardial segments were analyzed in each patient, and in all segments evaluated, segmental strain was analyzed in the automatic mode by the software and, if required, with manual correction of the segment limits by the echocardiographer responsible for the analysis.

Statistical analysis

Data were coded and entered into a Microsoft Excel™ database and were subsequently analyzed using the statistical package SPSS® version 20. A descriptive statistics was done to the variables chosen, resulting in the distribution of absolute and relative frequency of qualitative variables and the mean and standard deviation of the continuous quantitative variables. Then, we compared the means of the independent and dependent variables of the groups through the Student t test for quantitative variables. To determine the accuracy of the longitudinal strain variable for the presence of myocarditis on CMR, we built a ROC (receiver operating characteristic) curve and determined the AUC (area under the curve) with the respective confidence interval. On all tests, a probability of significance (p) smaller than 0.05 was used for rejection of a null hypothesis.

Results

The study evaluated 28 patients, including 82.1% (n = 46) males with a mean age of 35.6 ± 8.9 years. Mean left ventricular ejection fraction was 60.5 ± 5.8%. Of the 448 myocardial segments evaluated, 316 segments were normal (group 0) and 132 segments were diagnosed with myocarditis using delayed enhancement on CMR (group 1).

Regarding location, the inferolateral wall was the most affected (71.4%), followed by the lateral wall (64.3% - Figure 1) and inferior wall (57.1%).

Comparison of longitudinal strain between the groups with and without myocarditis showed a significant overall difference (-19.6 ± 2.9 vs. 15.4 ± 2.9, p = 0.001). Table 1 shows a comparative analysis between the 16 segments evaluated. In our sample, two-dimensional strain was able to evaluate all segments analyzed.

The accuracy of the strain in identifying delayed enhancement on CMR showed sensitivity and specificity of 75% and 79%, respectively, for a cutoff of 17.5 and AUC of 0.86 (95% CI 0.82 - 0.89) (Figure 2).

Discussion

Our study showed that the two-dimensional strain was able to discriminate normal cardiac segments from cardiac segments with signs of acute myocarditis on CMR, allowing differentiation even in the absence of myocardial contractile abnormalities on conventional echocardiography and CMR.

Contractility of the heart is highly complex due to the arrangement of myocardial fibers and ventricular myocardium may be divided into three layers: they present a predominantly longitudinal arrangement on the subendocardial layer, take on a circumferential shape on the midwall layer and show a longitudinal pattern on the epicardial layer.[5-7] Myocardial contractility is heterogeneous and subendocardial contraction is greater than the subepicardial contraction, therefore, the wall thickening seen in the analysis of contractility on echocardiography and cardiac magnetic resonance imaging predominantly reflects the involvement of the subendocardial fibers.[8] The existence of a pressure gradient is observed from the endocardium to the epicardium, being higher in the endocardium and smaller in the epicardium.[5] Furthermore, it is known that there is another tension gradient in the myocardium, being greater at the apex and smaller at the base.[9] This pattern suggests that the abnormalities found in the myocardium, particularly in areas with smaller tension, may not affect the left ventricular ejection fraction.

Acute myocarditis shows a pattern of lesions predominantly affecting the subepicardial layer, particularly in less serious cases.[10] The subendocardial lesions, on the other hand, are more related to the presence of ischemia, as in myocardial infarction.[11] Therefore, the involvement in myocarditis may be related to areas of smaller contribution to myocardial contraction, which explains the absence of contractile abnormality on echocardiography and cardiac magnetic resonance imaging, especially in regional abnormalities.[12]

The two-dimensional strain, through the speckle tracking mode, evaluates quantitative indices of intrinsic cardiac strain, providing a quantitative assessment of the regional and global contractility on the longitudinal, radial and circumferential planes.[4,13] Longitudinal strain predominantly relates to the subendocardial fibers. This contribution can be proven by the reduction of longitudinal strain in patients with subendocardial infarction almost identical to transmural infarction.[14,15] However, this study shows longitudinal strain abnormalities without involvement of the subendocardial plane, which can be explained by the complex orientation of the myocardial fibers.[16] During ventricular ejection, the heart volume is reduced due to contraction of the subendocardial and subepicardial fibers. The involvement of either of these fibers (subendocardial involvement in ischemia and subepicardial involvement in focal myocarditis) may lead to a reduction of longitudinal strain. These findings were corroborated in a study that showed a sensitivity of 78% and specificity of 93% for detection of myocarditis using the global longitudinal strain (GLS).[17] In another study, Hsiao et al.[18] demonstrated the prognostic and diagnostic value of GLS in patients with myocarditis, even with normal ejection fraction.

Limitations

One limitation of this study is that it was conducted at one service only and with a small number of patients. The reference standard for the diagnosis of myocarditis is endomyocardial biopsy, however, this method is invasive and not free from complications, and CMR has been widely used for the diagnosis of myocarditis. Evaluation of radial and circumferential strain was not used in our study because of greater variability and limited use of these techniques in clinical practice.

Conclusion

Patients with acute myocarditis with subepicardial involvement and no evidence of change of myocardial motility may present abnormalities in longitudinal strain, and this technique can be useful in the diagnostic evaluation of these patients. Further studies with larger number of patients are needed to confirm the value of these findings in clinical practice.

Authors' contributions

Research creation and design: Barros MVL, Siqueira MHA, Silva FJM, Santos IP, Reis LM, Silva PHC, Ornelas CE; Data acquisition: Barros MVL, Siqueira MHA, Silva FJM, Santos IP, Reis LM, Silva PHC, Ornelas CE; Data analysis and interpretation: Barros MVL, Ornelas CE; Statistical analysis: Barros MVL; Manuscript drafting: Barros MVL, Silva FJM, Santos IP, Silva PHC, Ornelas CE; Critical revision of the manuscript as for important intellectual content: Barros MVL, Siqueira MHA, Silva FJM, Santos IP, Reis LM, Silva PHC, Ornelas CE.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

Sources of Funding

This study had no external funding sources.

Academic Association

This study is not associated with any graduate program.

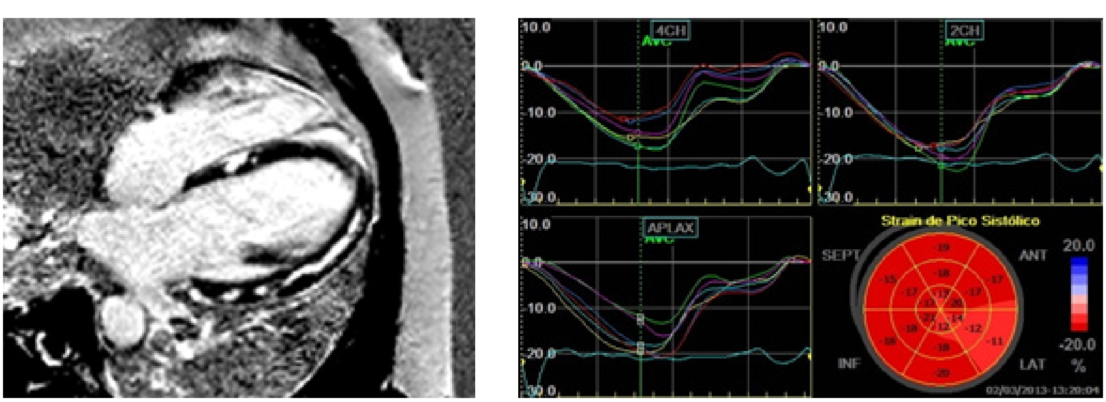

Figure 1 – *Patient with acute myocarditis presenting (A) cardiac magnetic resonance imaging with midwall delayed enhancement on lateral wall and (B) reduction of longitudinal strain on the lateral wall. .*

Table 1 – Statistical analysis of 16 myocardial segments in 28 patients with myocarditis

Segment	Group 0	Group 1	p
Anterior Basal	-18.42 ± 2.1	-15.00 ± 1.1	0.006
Anteroseptal basal	-18.75 ± 1.9	-15.00 ± 2.3	0.002
Inferoseptal basal	-17.50 ± 1.8	-12.00 ± 3.4	0.000
Inferior basal	-16.50 ± 4.77	-12.33 ± 4.6	0.029
Inferolateral basal	-18.50 ± 1.9	-13.83 ± 1.1	0.000
Anterolateral basal	-18.20 ± 1.7	-16.25 ± 3.4	0.056
Anterior medial	-21.00 ± 3.5	-18.33 ± 1.3	0.084
Mid anteroseptal	-20.82 ± 4.0	-18.00 ± 1.7	0.116
Mid inferoseptal	-19.50 ± 2.2	-15.00 ± 1.0	0.000
Mid inferior	-18.14 ± 4.4	-16.43 ± 2.0	0.200
Mid inferolateral	-16.17 ± 3.5	-17.25 ± 3.9	0.460
Mid anterolateral	-18.33 ± 3.1	-18.60 ± 3.3	0.833
Apical anterior	-21.00 ± 1.4	-20.38 ± 3.3	0.801
Apical septal	-21.83 ± 2.6	-14.00 ± 4.6	0.000
Inferior apical	-19.22 ± 3.3	-18.40 ± 2.5	0.510
Apical lateral	-19.14 ± 4.8	-17.00 ± 3.1	0.177
Medium strain	-19.57 ± 2.8	-15.43 ± 2.8	0.000

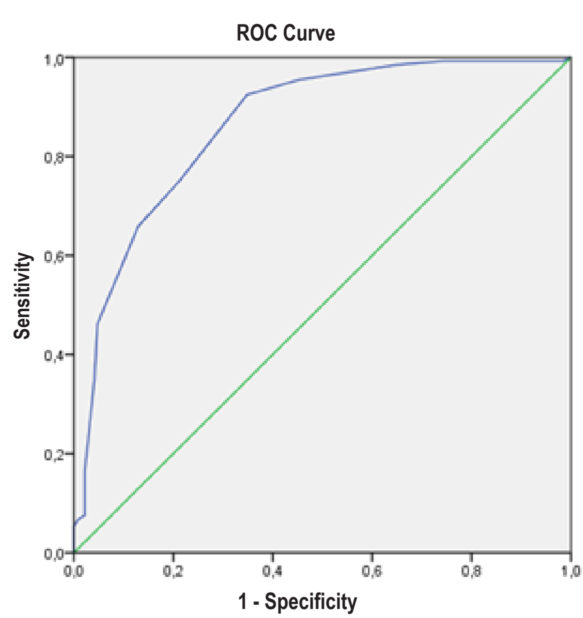

Figure 2 – *Graphical representation of sensitivity and specificity of strain through the ROC curve.*

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