Review Article

Use of Three-Dimensional Echocardiography in the Analysis of Ventricular Function in Chagas Disease

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Abstract

Chagas disease is recognized as a global public health issue, capable of causing cardiac, digestive, and neurological manifestations. The echocardiogram is a fundamental complementary exam in assessing patients with cardiac involvement, evaluating various parameters of cardiac structure and function. This review aims to discuss the use of three-dimensional echocardiography in analyzing ventricular function in patients with Chagas disease.

Introduction

Chagas disease, caused by the protozoan *T. cruzi*, is mainly transmitted by vectors, through the inoculation into the skin from feces of triatomines that have been previously infected after sucking the blood of contaminated people or animals. It can also be transmitted orally, transplacentally, by transfusion of blood and blood products, by solid organ transplantation, or by accidents with biological material.[1-3]

It is estimated that approximately 6 to 7 million people are infected worldwide, mainly in Latin American countries. However, in recent years, with the increase in migratory flow from rural to urban areas and from endemic countries to non-endemic countries, this pathology has been recognized as a global public health problem.[3]

Its natural history involves an acute phase, which is not always symptomatic and may last from a few weeks to a few months, and a chronic phase, which can manifest with cardiac, digestive, or neurological impairment. Cardiac involvement represents the most feared manifestation, characterized by complications with high morbidity and mortality, such as heart failure, arrhythmias, and stroke.[1,2,4]

In this scenario, echocardiography is the most commonly used complementary exam for assessment and follow-up of patients with Chagas disease, making it possible to analyze cardiac structure and function, detect intracavitary thrombi, and assess secondary valve involvement.[1,5] In recent years, new techniques, such as three-dimensional (3D) echocardiography and the assessment of myocardial strain using the speckle-tracking method have shown to be promising in the assessment of cardiac mechanics in various clinical scenarios. [6-14]

The objective of this review is to discuss the use of 3D echocardiography in the analysis of ventricular function in patients with Chagas disease.

Keywords

Echocardiography, Three-Dimensional; Chagas Cardiomyopathy; Ventricular Function.

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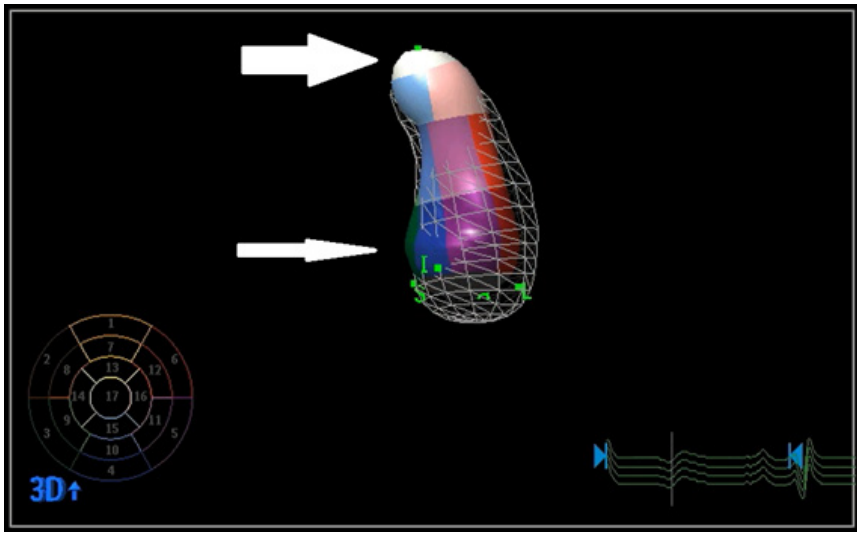
Assessment of left ventricular function by 3D echocardiography

In patients with Chagas disease, segmental involvement is a marker of unfavorable prognosis, which has already been demonstrated in diverse studies. The most characteristic segmental changes occur in the inferior, inferolateral, and apical segments of the left ventricle (LV). [4,6,15-17] These segments are not always adequately assessed on two-dimensional (2D) studies, due to image shortening (which can exclude the apical segments from analysis) or to not including segments in the quantification of global function of Simpson's biplane method (which does not encompass the inferolateral segments).[6] Assessment of left ventricular ejection fraction (LVEF) is one of the main parameters for classification and staging of patients with Chagas disease; therefore, it is recommended to use methods that show high accuracy and reproducibility for estimating LVEF.[1,5,6]

3D echocardiography allows the calculation of ventricular volumes, without requiring estimation using geometric formulas, as is the case with 2D echocardiography.[13] Furthermore, it has demonstrated greater reproducibility and accuracy in calculating volumes compared to cardiac magnetic resonance, and the method is increasingly used in diverse cardiomyopathies.[11,13,18,19] Regarding advantages in relation to other modalities, we can highlight that it the method is less cumbersome, non-invasive, more portable, not related to radiation exposure, and capable of obtaining images with shorter acquisition time and better temporal resolution. However, compared to 2D echocardiography, 3D echocardiography has some limitations related to cost, availability, spatial resolution, and technical difficulties, especially in patients with irregular heart rhythm, such as atrial fibrillation.[10,13,19]

In spite of the greater accuracy of 3D echocardiography in comparison to 2D for analysis of ventricular volumes and LVEF in different clinical scenarios, its prognostic superiority still remains uncertain.[6] In a single-center observational study conducted with 172 patients with ischemic and non-ischemic dilated cardiomyopathy who were candidates for therapy with an implantable cardioverter defibrillator (ICD), 3D LVEF

Central Illustration: Use of Three-Dimensional Echocardiography in the Analysis of Ventricular Function in Chagas Disease



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3D rendering of left ventricular volume during systole in a patient with Chagas disease, showing large apical aneurysm formation (thick arrow), as well as minor basal inferior septal dyskinesia (thin arrow).

proved to be an independent predictor of major arrhythmic events, suggesting that 3D LVEF could change the decision to implant an ICD in this scenario, where up to 20% of patients could be reclassified below the indication threshold for ICD implantation when using the 3D method.[20] A recent single-center study with 725 patients referred for routine echocardiographic evaluation also found that 3D LVEF had an incremental value for predicting composite outcomes, in relation to 2D LVEF. Furthermore, the partition values for mild, moderate, and severe reduction in LV systolic function on the 3D method demonstrated greater discriminatory power for cardiac death than the 2D values, and LV dilation defined by 3D volume showed a greater association with mortality.[21]

In addition to the absolute assessment of ventricular volumes and 3D LVEF, it is also possible to obtain a volume-time curve corresponding to the dynamic changes in LV volume during the cardiac cycle.[22] Analysis of this curve makes it possible to assess new non-invasive parameters of ventricular performance, such as maximum systolic flow, peak flow during early LV filling, and peak flow during left atrial contraction.[23,24] A recently published cross-sectional study, involving 20 patients with Chagas disease and 15 healthy individuals, aimed to characterize these parameters in patients with Chagas disease. In that study, patients with Chagas disease had maximum systolic flow, peak flow during early LV filling, and peak flow during atrial contraction similar to patients in the control group, thus demonstrating, in a non-invasive manner, that the increase in LV end-diastolic volume was the main adaptive mechanism that made it possible to maintain flow and stroke volume in patients with severe LV systolic dysfunction.[25]

Notwithstanding the increasing use of 3D echocardiography to estimate volumes and LVEF in various pathologies, to our knowledge, there are no studies that have specifically evaluated the superiority of 3D echocardiography in relation to 2D echocardiography in patients with Chagas disease, in relation to diagnostic capacity, classification in degrees of left ventricular systolic dysfunction, or in terms of prognosis of major cardiac outcomes, such as ventricular arrhythmias or mortality.

Assessment of right ventricular function by 3D echocardiography

In patients with Chagas disease, involvement of the right ventricle (RV) may occur early in the natural history of the disease, affecting patients with the indeterminate and digestive form of Chagas disease.[1,5,26-29]

Assessment of the RV by 2D echocardiography poses a series of challenges. [13,30,31] The RV has a more complex geometric formation than the LV, with at least 6 distinct morphological regions: inflow tract, outflow tract, apex (septal and free wall regions), and body (septal and free wall regions).[32] Furthermore, the RV has other characteristics that make it difficult to assess using the 2D method, for example, a very thin myocardial wall, the presence of prominent trabeculations, and a greater arrangement of endocardial fibers in the longitudinal direction. For these reasons, 2D echocardiography analysis is performed in an integrated manner, obtaining various geometry and function parameters.[13,30,31,33]

Accordingly, 3D echocardiography has been increasingly used to analyze RV systolic function. By means of specific

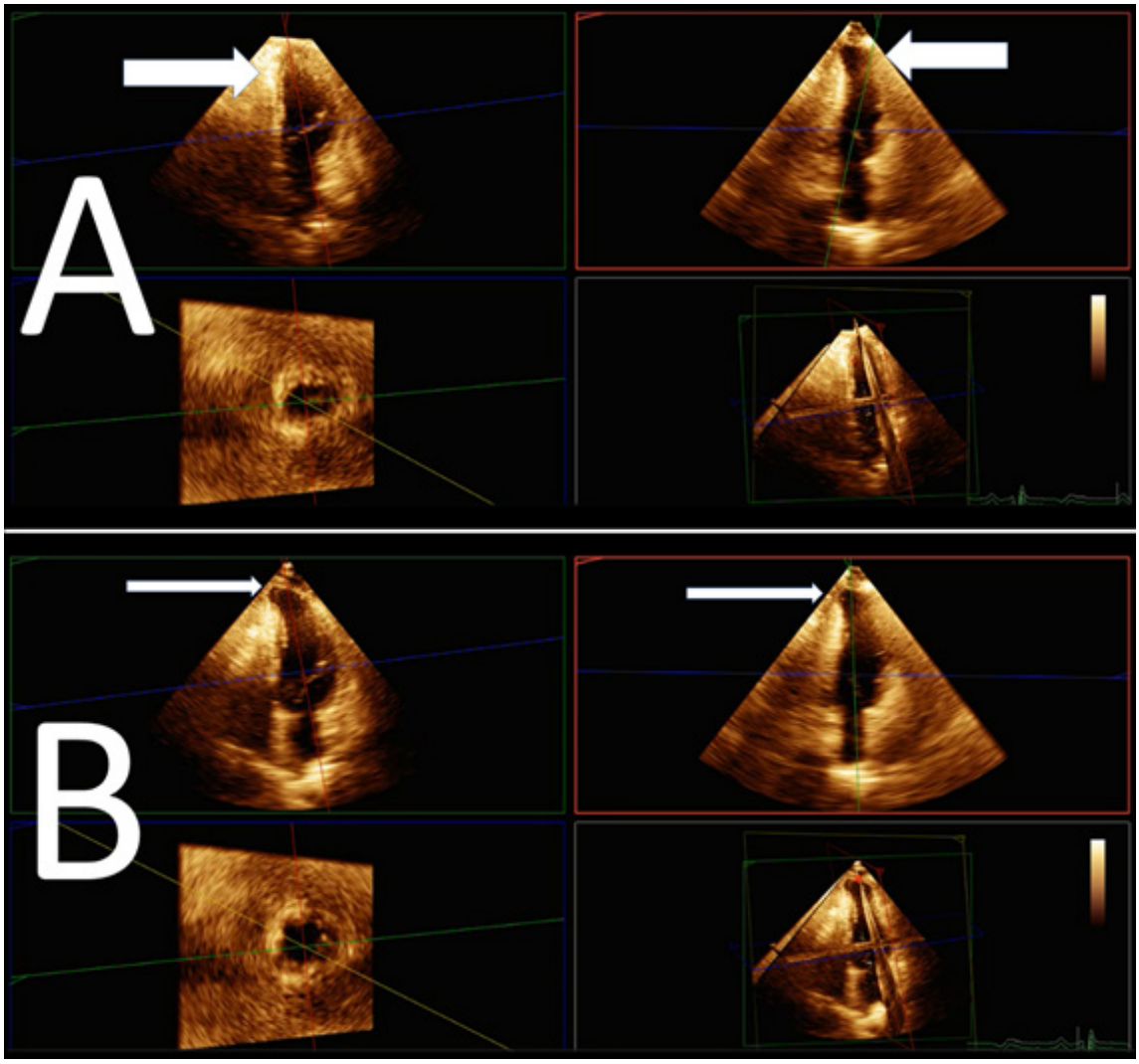

Figure 1 – *Multiplanar images derived from 3-dimensional acquisition in a patient with Chagas disease. Panel A – Notable shortening of the left ventricular apex (thick arrows). In this case, the assessment of ventricular volumes may be inaccurate. Panel B – After adjusting the planes, it was possible to identify the true apex with the inclusion of a large apical aneurysm in the analysis of ventricular volumes (thin arrows).*

software designed to evaluate the RV, it is possible to assess right ventricular ejection fraction (RVEF) and volumes, showing good correlation with cardiac magnetic resonance.[12,34,35]

3D echocardiography can also be used to characterize RV geometry, and it is a promising method for assessing RV remodeling.[32] Previous studies conducted in patients with pulmonary hypertension and tetralogy of Fallot have demonstrated differences in RV remodeling according to the etiology of RV overload.[36,37]

In recent years, some studies have demonstrated the additional prognostic value of analyzing RV systolic function with the use of 2D echocardiography. Nagata et al. found that 3D echocardiography showed high accuracy in relation to cardiac magnetic resonance in the assessment of RVEF and volumes. It was also demonstrated that 3D RVEF was independently associated with cardiac outcomes in diverse etiologies of RV dysfunction.[6] In an observational study including 394 patients with heart disease, Surkova et al. demonstrated that 3D RVEF was associated with mortality ($p < 0.0001$).[38] Kitano et al. published a meta-analysis that demonstrated that RVEF < 45% was associated with worse cardiovascular outcomes, both in individuals with normal LVEF and in those with reduced LVEF. In the same study, subgroup analysis revealed that RVEF had prognostic value both in patients with pulmonary hypertension and in those with cardiovascular disease. Univariable Cox proportional analysis revealed that 3D RVEF was associated with both cardiac death ($p < 0.0001$) and major adverse cardiovascular events ($p < 0.0001$). 3D RVEF remained an independent predictor of cardiac death ($p < 0.0001$) and

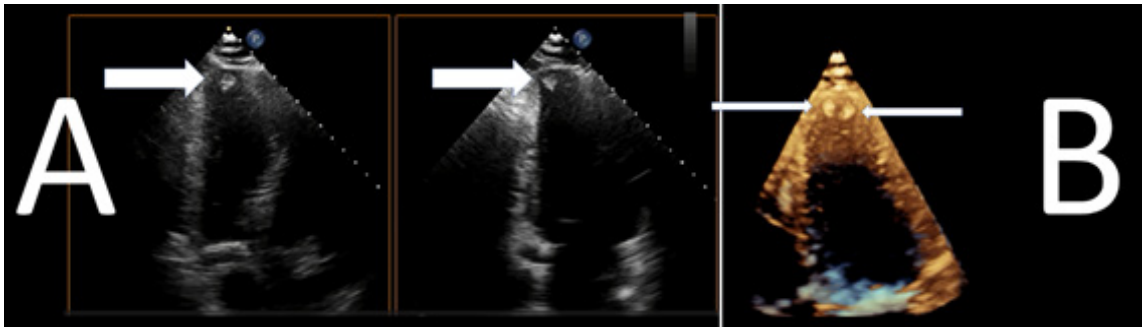

Figure 2 – *Assessment of intracavitary thrombi in a patient with Chagas disease. Panel A – Orthogonal images obtained through simultaneous biplanar evaluation. Panel B – 3D image showing 2 apical thrombi.*

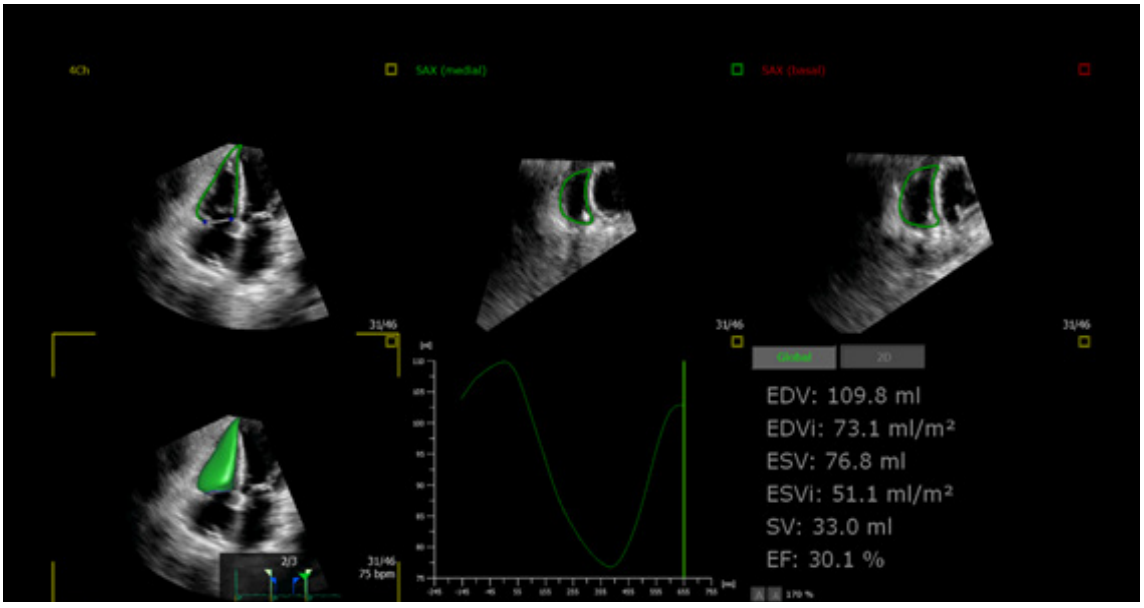

Figure 3 – *3D assessment of right ventricular function in a patient with Chagas disease. The RVEF was calculated to be 30%. EDV: End-Diastolic Volume; EDVi: Indexed End-Diastolic Volume; ESV: End-Systolic Volume; ESVi: Indexed End-Systolic Volume; SV: Stroke Volume; EF: Ejection Fraction.*

major adverse cardiovascular events ($p < 0.0001$), even after multivariable Cox proportional hazard analysis.[39]

In spite of initial evidence of the additional value of 3D echocardiography in some clinical conditions, to date there are no studies characterizing changes in RV size, geometry, and function using this method in patients with Chagas disease.

Assessment of 3D myocardial strain

In recent years, the assessment of cardiac mechanics using the speckle-tracking method has proven to be a promising tool in the assessment of myocardial dysfunction. There are several studies demonstrating the ability of global longitudinal strain analysis to predict severe events, such as mortality and composite outcomes.[40,41]

Even though the role of speckle-tracking echocardiography in detecting regional changes in patients with Chagas disease, even in more subtle forms, has already been demonstrated, it is not possible to confirm that the changes are correlated with the presence of myocardial fibrosis,[42,43] as they may be manifestations of altered strain even before fibrotic replacement. More recently, it has been proposed that 3D myocardial strain analysis would have additional prognostic value, and several indices can be obtained using this tool.[41,44]

A recent study including 72 patients with Chagas disease aimed to characterize new echocardiographic variables according to LVEF and to evaluate their role in predicting clinical outcomes in patients with Chagas disease.[45] In this study, the feasibility of acquiring LV strain was high (91.5% in patients with LVEF < 40%; 89.4% in patients

with LVEF ≥ 40% and < 50%; 88% in patients with LVEF ≥ 50%), even though it was inferior to the feasibility of 2D strain (99.3%, 98.9%, and 100%, respectively). After regression analysis using the Cox model, the parameters derived from 3D strain that proved to be predictors of composite outcomes (hospitalization for heart failure, complex ventricular arrhythmias, heart transplantation, and death) were 3D global longitudinal strain and 3D LV area strain.[45] In particular, 3D LV area strain is a very promising index that quantifies change in the endocardial area, integrating longitudinal and circumferential deformation, allowing more detailed assessment of the different types of myocardial fibers and making it possible to better understand the pathophysiology of cardiomyopathies.[41] However, a recent study of patients with ischemic and non-ischemic cardiomyopathy did not find an incremental value for 3D strain in comparison with analysis of LVEF.[46]

Conclusion

Chagas disease is a global public health problem with elevated morbidity and mortality, mainly due to cardiac involvement of the disease. There are several theoretical advantages to the use of 3D echocardiography in patients with Chagas disease due to characteristics that are intrinsic to the method and to the pathology. However, in patients with Chagas disease, the additional value of 3D echocardiography in relation to 2D echocardiography still needs to be better clarified, by means of studies that also take into consideration the cost-effectiveness of the method.

Additional considerations

The data for this review were identified through database searches in the PubMed, Medline, Lilacs, and Scielo platforms. Articles published in Portuguese, English, and Spanish were accepted.

Author Contributions

Conception and design of the research, acquisition of data and writing of the manuscript: Barros-Filho ACL; analysis and interpretation of the data and critical revision of the manuscript for intellectual content: Barros-Filho ACL, Romano MMD.

Potential Conflict of Interest

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

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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