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Multimodality imaging evaluation of Chagas disease: an expert consensus of Brazilian Cardiovascular Imaging Department (DIC) and the European Association of Cardiovascular Imaging (EACVI)

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Aims

To develop a document by Brazilian Cardiovascular Imaging Department (DIC) and the European Association of Cardiovascular Imaging (EACVI) to review and summarize the most recent evidences about the non-invasive assessment of patients with Chagas disease, with the intent to set up a framework for standardized cardiovascular imaging to assess cardiovascular morphologic and functional disturbances, as well as to guide the subsequent process of clinical decision-making.

Methods and results

Chagas disease remains one of the most prevalent infectious diseases in Latin America, and has become a health problem in non-endemic countries. Dilated cardiomyopathy is the most severe manifestation of Chagas disease, which causes substantial disability and early mortality in the socially most productive population leading to a significant economical burden. Prompt and correct diagnosis of Chagas disease requires specialized clinical expertise to recognize the unique features of this disease. The appropriate and efficient use of cardiac imaging is pivotal for diagnosing the cardiac involvement in Chagas disease, to stage the disease, assess patients' prognosis and address management. Echocardiography is the most common imaging modality used to assess, and follow-up patients with

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Chagas disease. The presence of echocardiographic abnormalities is of utmost importance, since it allows to stage patients according to disease progression. In early stages of cardiac involvement, echocardiography may demonstrate segmental left ventricular wall motion abnormalities, mainly in the basal segments of inferior, inferolateral walls, and the apex, which cannot be attributed to obstructive coronary artery arteries. The prevalence of segmental wall motion abnormalities varies according to the stage of the disease, reaching about 50% in patients with left ventricular dilatation and dysfunction. Speckle tracking echocardiography allows a more precise and quantitative measurement of the regional myocardial function. Since segmental wall motion abnormalities are frequent in Chagas disease, speckle tracking echocardiography may have an important clinical application in these patients, particularly in the indeterminate forms when abnormalities are more subtle. Speckle tracking echocardiography can also quantify the heterogeneity of systolic contraction, which is associated with the risk of arrhythmic events.

Three-dimensional (3D) echocardiography is superior to conventional two-dimensional (2D) echocardiography for assessing more accurately the left ventricular apex and thus to detect apical aneurysms and thrombus in patients in whom ventricular foreshortening is suspected by 2D echocardiography. In addition, 3D echocardiography is more accurate than 2D Simpson's biplane rule for assessing left ventricular volumes and function in patients with significant wall motion abnormalities, including aneurysms with distorted ventricular geometry. Contrast echocardiography has the advantage to enhancement of left ventricular endocardial border, allowing for more accurate detection of ventricular aneurysms and thrombus in Chagas disease.

Diastolic dysfunction is an important hallmark of Chagas disease even in its early phases. In general, left ventricular diastolic and systolic dysfunction coexist and isolated diastolic dysfunction is uncommon but may be present in patients with the indeterminate form. Right ventricular dysfunction may be detected early in the disease course, but in general, the clinical manifestations occur late at advanced stages of Chagas cardiomyopathy. Several echocardiographic parameters have been used to assess right ventricular function in Chagas disease, including qualitative evaluation, myocardial performance index, tissue Doppler imaging, tricuspid annular plane systolic excursion, and speckle tracking strain.

Cardiac magnetic resonance (CMR) is useful to assess global and regional left ventricular function in patients with Chagas diseases. Myocardial fibrosis is a striking feature of Chagas cardiomyopathy and late gadolinium enhancement (LGE) is used to detect and quantify the extension of myocardial fibrosis. Myocardial fibrosis might have a role in risk stratification of patients with Chagas disease. Limited data are available regarding right ventricular function assessed by CMR in Chagas disease.

Radionuclide ventriculography is used for global biventricular function assessment in patients with suspected or definite cardiac involvement in Chagas disease with suboptimal acoustic window and contraindication to CMR. Myocardial perfusion scintigraphy may improve risk stratification to define cardiac involvement in Chagas disease, especially in the patients with devices who cannot be submitted to CMR and in the clinical setting of Chagas patients whose main complaint is atypical chest pain. Detection of reversible ischemic defects predicts further deterioration of left ventricular systolic function and helps to avoid unnecessary cardiac catheterization and coronary angiography.

Conclusion

Cardiac imaging is crucial to detect the cardiac involvement in patients with Chagas disease, stage the disease and stratify patient risk and address management. Unfortunately, most patients live in regions with limited access to imaging methods and point-of-care, simplified protocols, could improve the access of these remote populations to important information that could impact in the clinical management of the disease. Therefore, there are many fields for further research in cardiac imaging in Chagas disease. How to better provide an earlier diagnosis of cardiac involvement and improve patients' risk stratification remains to be addressed using different images modalities.

Keywords

Chagas disease • Chagas cardiomyopathy • echocardiography • three-dimensional echocardiography • speckle tracking echocardiography • cardiac magnetic resonance • nuclear cardiology • radionuclide ventriculography • myocardial sympathetic innervation

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- Chronic form of Chagas cardiomyopathy evolving to heart failure carries higher mortality
- Impaired LV systolic function, New York Heart Association class III/IV, cardiomegaly, and non-sustained ventricular tachycardia are important predictors of poor prognosis in patients with chronic Chagas disease

LV systolic function

Echocardiography

Echocardiography is the most commonly used imaging modality for assessment and follow-up of patients with Chagas disease.⁴¹ Echocardiography allows to stage patients (A, B, C, and D) according to international recommendations adapted to the Chagas disease (Table 1).^{17,41} In early stages of cardiac involvement, echocardiography may demonstrate segmental LV wall motion abnormalities and diastolic dysfunction.^{4,42,43} The most commonly involved LV regions are the basal inferior and inferolateral walls (Figure 2; Supplementary

Videos 1 and 2), and the apex, which cannot be attributed to obstructive coronary artery.⁴⁴ Wall motion abnormalities can be detected in more than one wall in the same patient. The extent of regional wall motion abnormality varies from hypokinesis to akinesis and aneurysm. The presence of segmental abnormalities identifies individuals at risk of further LV function global deterioration.⁴⁵

Wall motion abnormalities can be found in around 10% of patients in the early stages of cardiac involvement and they can be associated with ventricular arrhythmias.⁴⁶ As the disease progresses to LV dilatation and dysfunction, the prevalence of segmental wall motion abnormalities increases to about 50% of patients.^{47,48}

Detection of regional wall motion abnormalities by visual assessment is subjective and highly dependent on the skills of the interpreter. Moreover, subtle changes in segmental contractility may be missed by visual assessment. Strain measurement using speckle tracking echocardiography is a new method that allows a more precise and quantitative measurement of the regional myocardial function, overcoming the subjective evaluation by conventional echocardiography (Figures 3 and 4).^{49,50} Since segmental wall motion abnormalities are frequent in Chagas disease, speckle tracking echocardiography may have an important clinical application in these patients, particularly in the indeterminate forms when abnormalities are more subtle. A study including 125 patients with Chagas disease found that global longitudinal, circumferential, and radial LV strain were reduced in the patients who had cardiac fibrosis on CMR despite normal global and segmental LV systolic function by echocardiography.⁵¹ Specifically, the patients with fibrosis had lower radial LV strain in the basal inferoseptal wall than patients without cardiac fibrosis ($27 \pm 17\%$ vs. $60 \pm 15\%$).

Speckle tracking echocardiography can also quantify the heterogeneity of systolic contraction, which is associated with the risk of arrhythmic events. A recent study showed that mechanical dispersion was associated with malignant ventricular arrhythmias in patients with CCM independent of LV ejection fraction (Figure 5).⁵²

LV apical aneurysms are a typical finding in patients with CCM and can be helpful in making the aetiologic diagnosis in dilated cardiomyopathy (Figure 6; Supplementary Videos 3 and 4).^{4,44,47} This abnormality may be missed if only conventional apical views are acquired.

Table 2 Score for predicting all-cause mortality in Chagas disease (Rassi's score)³⁰

Predictors	Points		
New York Heart Association class III or IV	5		
Cardiomegaly (chest X-ray)	5		
Segmental or global wall motion abnormality (echo)	3		
Non-sustained ventricular tachycardia (24 h Holter)	3		
Low QRS voltage (ECG)	2		
Male sex	2		
Risk category	5-years mortality	10-years mortality	Total points
Low	2%	10%	0–6
Intermediate	18%	44%	7–11
High	63%	84%	12–20

ECG, electrocardiogram.

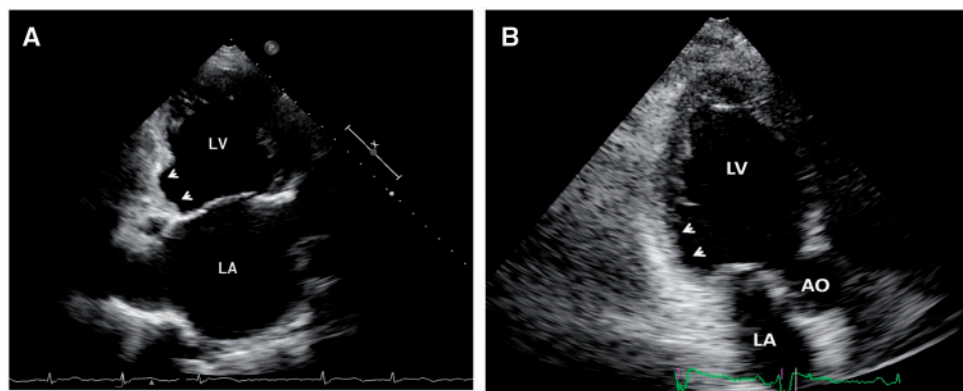


Figure 2 (A) Apical two-chamber view 2D echocardiographic image showing akinesis of the basal segment of the inferior wall. (B) Apical long-axis view showing akinesis of the basal segment of the inferolateral wall.

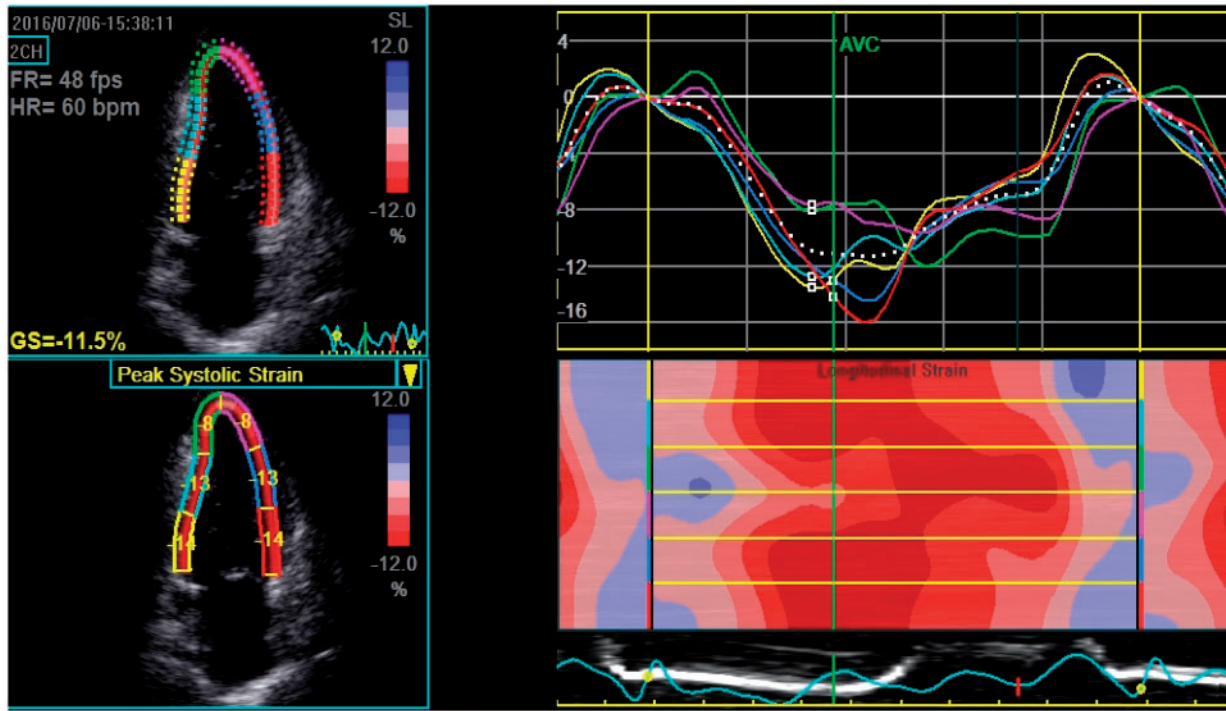


Figure 3 Left ventricular longitudinal strain at apical two-chamber view (left, upper panel) in an asymptomatic patient with Chagas disease and normal global left ventricular ejection fraction. The regional strain values are displayed both as regional strain (left, lower panel) and time curves (right, upper panel) as well as in an M-mode parametric colourization (right, lower panel). AVC, aortic valve closure.

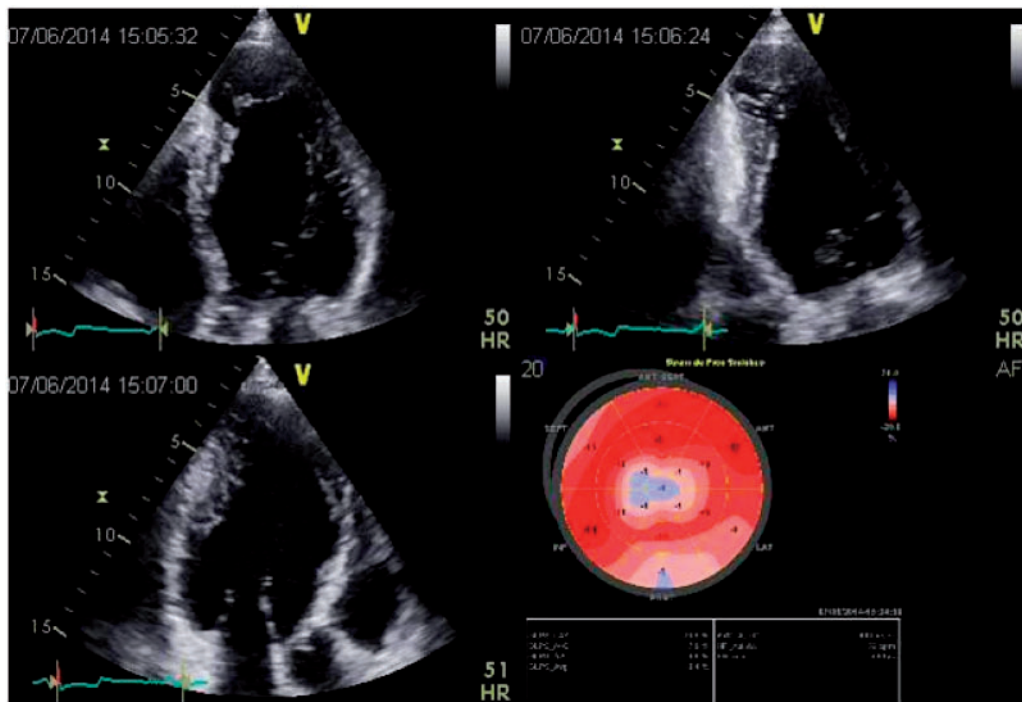


Figure 4 Computation of peak LV global longitudinal strain by using the speckle tracking technique on three conventional apical views: four-chamber (left, upper panel), two-chamber (right, upper panel), and apical long axis (left, lower panel). LV segmental values of longitudinal strain are displayed both as numbers and as parametric colorization on a bull's eye display (right, lower panel). There is an apical aneurism that is seen in each view.

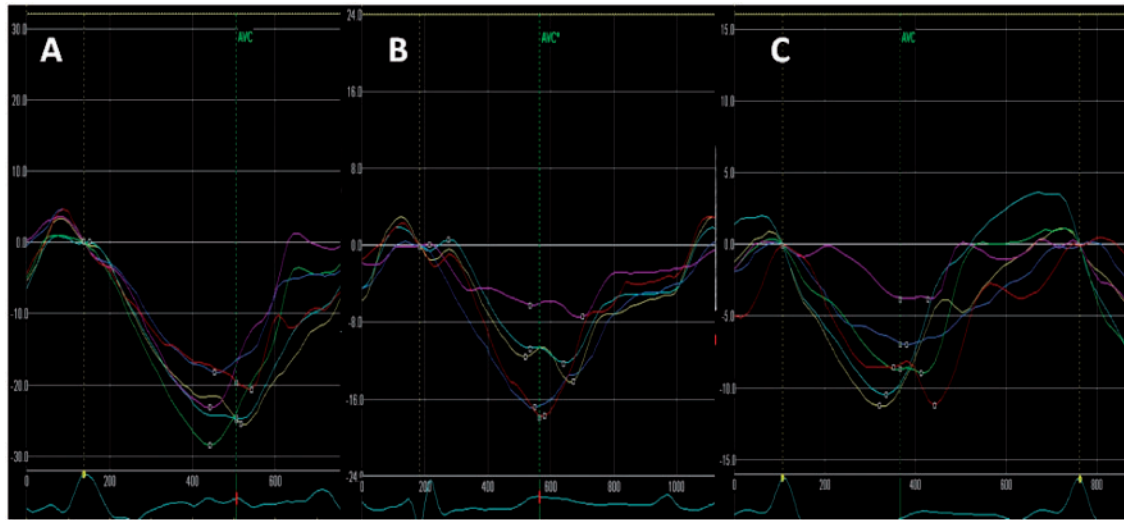


Figure 5 2D LV longitudinal strain in Chagas disease. Note the progressive decrease in LV longitudinal strain from patient in indeterminate form (A) to the patients with cardiac form of Chagas disease (B and C). Each figure depicts the LV longitudinal strain curves for each of 6 segments analysed at the four-chamber view.

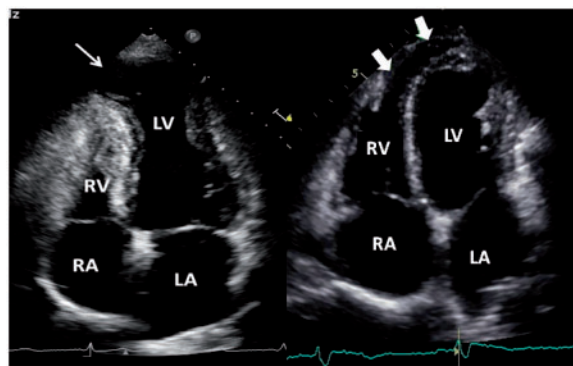


Figure 6 Apical four-chamber views showing left ventricular apical aneurysm (thin arrow, on the left), and right ventricular aneurysm (broad arrows, on the right) with a relatively normal left ventricle.

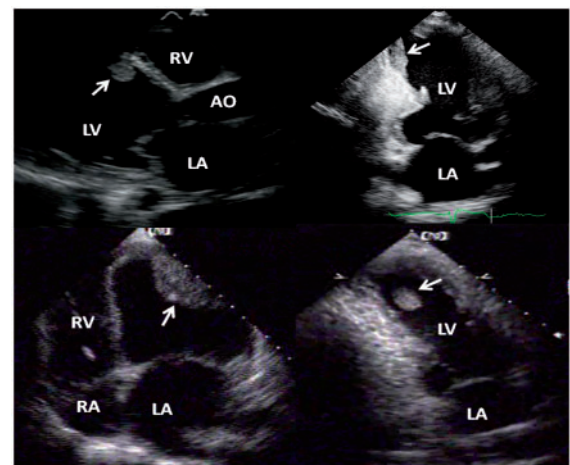


Figure 7 Echocardiographic images showing different locations of thrombus inside of the left ventricle.

In order to identify aneurysms, a careful examination requires not only standard views but also angulated apical views. Frequently, a modified four- and two-chambers views aiming posteriorly may be necessary to detect apical aneurysms and thrombus. The size of the aneurysm may range from small (like a ‘hollow punch’) to large with extensive wall thinning, similar to ischaemic aneurysms.^{44,47} Aneurysms are not limited to the apex or to the inferolateral wall,⁴⁴ they can also be found in interventricular septum and anterolateral walls, being more prevalent in patients with global LV systolic dysfunction.^{44,47} Previous studies using 2D echocardiography reported that the LV aneurysm prevalence was 8.5% (ranging from 1.6 to 8.6%) in asymptomatic patients but increased to 55% (ranging from 47 to 64%) in patients with moderate or severe LV global systolic

dysfunction.^{44,47,48} Right ventricular (RV) aneurysms are uncommon, but some patients have apical aneurysms affecting both ventricles (Figure 6; Supplementary Video 4). Intraventricular mural thrombi can be associated with aneurysms and are important risk factors for the occurrence of systemic embolisms including stroke^{35,36,53,54} (Figure 7; Supplementary movies 5 and 6).

Contrast echocardiography has the advantage to enhancement of LV endocardial border, allowing for more accurate detection of ventricular aneurysms and thrombus in Chagas disease.⁴⁴ With the apical four-chamber view, using contrast echo, it should be usually possible to clearly visualize the RV and LV cavities.

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