Learning objectives

The objective of this study is to present a brief review of the role of cardiac MRI in the diagnosis of myocarditis.
Background

• Myocarditis is defined as an inflammatory process affecting the myocardium. It is believed that the disease develops from pathological autoimmune response and viral infections.
• Its course is usually asymptomatic or insidious, with considerable difficulty in establishing the diagnosis, because of its nonspecific clinical presentation and the low sensitivity of additional tests.
• It is a clinical entity that is characterized by inflammatory infiltrates in the myocardium, with varying degrees of myocyte necrosis and engages adjacent parenchyma and interstitium of acutely or chronically.
• From the standpoint of topographical distribution of the inflammatory process, the infectious myocarditis may be focal, localized or diffuse.
• Histopathologically, it is classified as fulminant myocarditis, subacute and chronic.
• Studies suggest that myocarditis is a leading cause of sudden death that occurs in young adults under 40 years of age.
• The incidence and prevalence of myocarditis in the general population is unknown, it is estimated to reach about 8 to 10 people per 100,000. However, this value is considered underestimated due to lack of uniformity in the application of diagnostic criteria and the large number of asymptomatic cases.
• Although affecting children and adults, is a relatively uncommon finding in children, being more frequent in young people and in males at a ratio of 1.5:1 compared to females.

• Review the pathophysiology and clinical features in myocarditis:
• Etiologically, myocarditis may arise secondarily of various infectious diseases (which may have as agents viruses, bacteria, fungi and protozoa), of chemical, physical and pharmacological (adriamycin), by autoimmune mechanisms (rheumatic carditis) or by mixed processes (active myocarditis), where there is an initial viral infection followed by an assault to the immune myocyte. In 50% of cases, the etiology is unknown, ie, idiopathic.
• The viral etiology of myocarditis are the most prevalent. Viruses are the most frequently identified enteroviruses and adenoviruses, among the latter, there is the Coxsackie B. It is estimated that approximately 50% of viral myocarditis are caused by infection by Coxsackie B. Other viruses, such as cytomegalovirus, Epstein-Barr virus, parvovirus B19, among others, have been frequently implicated.
• Other causes of myocarditis include HIV infection, diphtheria, Chagas disease, dengue fever, Lyme disease and, more rarely, giant cell myocarditis of unknown etiology. Viral infections of the respiratory and gastrointestinal tract may involve the heart in up to 5% of patients.
• Pharmacological agents, for direct cytotoxic effect (lithium, cocaine, catecholamines, acetaminophen) or by hypersensitivity reactions (clozapine, penicillin, sulfonamides, hydrochlorothiazide, methyldopa) can also cause inflammation of the myocardium. Disorders of autoimmune nature, such as connective tissue diseases (systemic lupus erythematosus, rheumatoid arthritis, scleroderma), Churg-Strauss and hypereosinophilic syndrome, sarcoidosis and neoplasms were also associated with myocarditis.

• The symptoms of myocarditis is nonspecific and highly variable clinical presentation, ranging from asymptomatic forms, which can only be associated with electrocardiographic abnormalities, until signs and symptoms of acute heart failure, unspecified general malaise and even sudden cardiac death of unknown origin.

• In some cases it may manifest as chest pain syndromes of variable severity (which may simulate an acute coronary syndrome) or heart failure with hemodynamic compromise, dyspnea, palpitations, and mitral murmur.

• Sixty percent of the patients have a history of symptoms similar to a common cold. Thirty-five percent of patients with myocarditis and heart failure have chest pain.

• Of patients with asymptomatic ventricular dysfunction, 70% progress with worsening dysfunction.

• The diagnosis of myocarditis, in most cases, is fundamentally based on the high degree of clinical suspicion and confirmation by the findings in Cardiac MRI, which allows morphological characterization, analysis and visualization of functional parameters of tissue changes, and present high diagnostic accuracy (85%).

• The MRI cardiac is currently an important noninvasive diagnostic modality in the management of patients with clinically suspected myocarditis and is recognized as a method capable of providing valuable information that can not be obtained by other diagnostic methods.
Imaging findings OR Procedure details

- **The main techniques of cardiac magnetic resonance (CMR) and findings in the diagnosis of myocarditis.**

- The cardiac MRI can target for diagnosis of myocarditis mainly by two techniques. The first focused on the research of the inflammatory process, uses s T1 and T2 weighted image that can demonstrate increased signal intensity so early after contrast administration, allowing even monitor the inflammation in the myocardium.
- The second technique uses the delayed enhancement, being performed ten to fifteen minutes after contrast administration, which evaluates areas of necrosis and fibrosis.
- In cases of myocarditis, the presence of myocardial delayed enhancement may show focal necrosis or inflammatory lesion; involvement is often meso and / or epicardial (saving the subendocardial region), and regions are affected in a standard multifocal, heterogeneous, unrelated irrigation coronary territories.
- The typical finding of myocarditis in CMR is the presence of delayed enhancement in focal areas and not territorial. This finding can be found within seven days from the onset of infection.
- The delayed enhancement by CMR is usually positive in 88% to 95% of cases of myocarditis, which can detect inflammatory activity and serve to monitor the disease.
- The delayed myocardial enhancement technique is considered the best method for assessment of myocardial necrosis or fibrosis caused by myocardial infarction, acute or chronic, or other non-ischemic diseases such as myocarditis (Figure 1).
- Many studies show the importance of cardiac MRI in the diagnosis of both the acute and the chronic myocarditis.
- Cardiac MRI has a sensitivity of 80%, specificity of 95.5% and 85% diagnostic accuracy for the detection of acute myocarditis.

- This is a retrospective study, approved by the ethics committee and research HUCFF / FM / UFRJ under number 046/11-CEP. From May 2007 to March 2011, 724 Cardiac Magnetic Ressonance exams (CMR) were performed at two private institutions of Niterói, state of Rio de Janeiro, Brazil. The municipality of Niterói, is part of the Metropolitan Area II of the State of Rio de Janeiro, which covers a population of over 2 million people.
- The two institutions work independently but have the same medical team dedicated to the execution of CT and MRI exams, with the same protocols. The first institution is the Niterói Clinical Hospital (HCN) and the second is the institution Clinic ProEcho-Niterói. HCN is a tertiary hospital care
enabled to high complexity, with reference to multiple trauma, cardiac and neurological diseases, surgeries and organ transplants in eastern Rio de Janeiro. The ProEcho-Niterói is a clinic specializing in diagnostic imaging in the same region, serving mainly outpatients and inpatients as well, including units outside the municipality.

- In this study, 101 patients had myocarditis proven clinical and laboratory. Among this group, characterize the ones who were admitted in the Coronary Care Unit / ICU of HCN (Niterói Clinical Hospital), Rio de Janeiro, Brazil, and who were followed and treated clinically.
- The routine examinations at both institutions follows the same protocols. The standard methodology pre-examination, in order to achieve the best quality possible, is the explanation of the procedure to the patient to be submitted, and your understanding and cooperation very important. All patients signed an informed consent form with a full explanation of the tests and possible risks in procedures.
- The exams are performed with the patient supine, in a static position, with your arms close to your body aligned and instructed to perform end-expiratory apnea when necessary, and do not run, no movement during acquisition the images.
- The exams were conducted in the HCN a 1.5 Tesla Magnetom Symphony® (Siemens Medical Solutions, Erlangen, Germany) with gradients of low performance (23 mT amplitude and slew rate of 150T/m/s) cardiac coil-type phased-array with 4 elements, coupled with the electrocardiogram (ECG) and expiratory apnea, respiratory aided trigger.
- ProEcho clinical exams were performed on a 1.5 Tesla GE Signa Horizon® (General Electric, Milwaukee, USA) with high-performance gradients (32 mT amplitude and slew rate of 150T/m/s), cardiac coil-type phased-array with 4 elements, coupled to the ECG and expiratory apnea, respiratory aided trigger.
- In all exams we used paramagnetic contrast medium. The dose of the contrast medium was 0.2 ml / kg, this being injected through an infusion pump at a rate of 5 ml / s.

**Protocol of Cardiac MRI examinations performed in this study:**

1. Localizer 3 orthogonal planes, gradient echo T1 expiratory apnea.
2. Gradient echo sequence with steady-state free precession (SSFP) in expiratory apnea in the axial coupling without the electrocardiogram for analysis of the mediastinum.
3. SSFP Localizer (pseudo-axis two heart chambers) coupled to ECG in expiratory apnea.
4. SSFP Localizer (pseudo-axis two heart chambers) coupled to ECG in expiratory apnea.
5. Cine SSFP four chambers coupled to the ECG in expiratory apnea.
6. Cine SSFP short axis coupled to the ECG in expiratory apnea.
7. Inversion recovery sequences double-plane short axis.
8. Inversion recovery sequences triple-plane short axis.
10. SSFP sequence coupled to the ECG in expiratory apnea for planning radial planes where two long axes two cameras, a four-chamber long-axis and an outflow of the left ventricle are obtained.

• With regard to clinical examinations of patients who underwent MRI exams in this period, it was identified that the main indication was to detect myocardial ischemia with pharmacological stress, a total of 367 (51%) examinations, followed by evaluation diagnosis of myocarditis, 101 (14%).

• Of our 101 patients with myocarditis, 37(36.6%) had normal examinations and 64 (63.4%) had lesions evidenced by CMR.

• Among patients with myocarditis, 64 (63.4%) examinations showed signs indicative of an inflammatory process in the analysis of delayed enhancement, and 55 (85.9%) were performed as the first diagnostic test and 9 (14.1%) were control examinations. One of these patients had imaging characteristics compatible with Chagas disease (Figures 2-5).

• When analyzing the age distribution of patients with myocarditis, found a higher prevalence in the third and fifth decades of life.

• The multifocal pattern of myocardial delayed enhancement has a specificity of 96% and 76% sensitivity in the diagnosis, putting cardiac MRI as one of the first choices in the investigation of myocarditis.

• In our study, about half of patients referred with this specific indication had imaging findings consistent with myocarditis, and the examination also indicated for monitoring of disease in nine patients, all improved, among them one with complete remission.

• Until today, the prevalence of myocarditis is difficult to establish because of the difficulty of confirming the diagnosis by noninvasive methods, that will certainly change with the use of Cardiac MRI.

• The Brazilian Society of Cardiology has a Guideline to indicate exams MRI Cardiac and Cardiovascular Computed Tomography. In this Guideline, the myocarditis is included in Class IIa: "conditions in which there is level evidence/opinion is in favor of its use/efficacy".

• The American College of Cardiology considers the CMR, currently, as the noninvasive method of choice in the diagnosis and follow-up of patients with suspected myocarditis.
Fig. 1: Patterns of myocardial delayed enhancement and main differential diagnoses.

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**Fig. 2:** Female patient, 24 years old, with clinical and myocardial delayed enhancement pattern consistent with myocarditis. Delayed enhancement areas at the lateral basal segments and anterior and inferior wall (arrows). Short axis image (a) and long-axis two chambers (b).

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**Fig. 3:** Images acquisition with ECG-gate. Delayed enhancement on two chamber, long axis views (A,B) and left ventricle outflow tract plane (C). Note the presence of delayed enhancement foci and areas (arrows) in mesocardial and epicardial regions, always without involvement of the endocardial border (site of coronary disease) in inferolateral basal, anterior and inferoapical, anterolateral medial, lateral and septoapical segments, compatible with the presence of myocardial lesion.

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Fig. 4: Diffuse epimesocardial delayed enhancement with non coronary distribution.

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Fig. 5: Lateral basal wall delayed enhancement in a Chagas disease patient.

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Conclusion

- It is possible to consider MRI the method of choice for the diagnosis and management of patients with clinically suspected myocarditis.
- The pattern of patch late enhancement in CMR localized in meso and subepicardial areas are highly sensitivity and specific for the diagnosis of myocarditis.
- The multifocal pattern of delayed enhancement along with increased signal on MRI, especially in the acute phase of the disease, shows high rates of specificity and sensitivity, and can be considered as the method of choice for diagnosis and follow-up of patients with clinically suspected myocarditis, the accurate detection of areas of myocardial fibrosis and edema, with ample basis in medical literature.
References


2. Al-Amoodi, M; Rao, K; Rao, S; Brewer, JH et al. Fulminant Myocarditis Due to H1N1 Influenza. *Circ Heart Fail.*; 3:e7-e9, 2010.


