Roberto Kalil Filho, Cicero Piva de Albuquerque

Magnetic resonance imaging in Chagas' heart disease

Heart Institute, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo - São Paulo, Brazil

Many important aspects of Chagas' heart disease can be successfully assessed using magnetic resonance imaging of the heart. It is possible to obtain with great detail the anatomic characterization of the cardiac chambers as well as important information of the functional or metabolic status of the heart. Magnetic resonance imaging after gadolinium infusion seems also a promising technique to obtain a better regional characterization of myocardial tissue, and may be important in the non-invasive diagnosis of active myocarditis in patients with Chagas' heart disease.

UNITERMS: Chagas' disease. Myocarditis. Magnetic resonance imaging.

agnetic resonance imaging has become a powerful tool to increase the ability of the physician to achieve a precise diagnosis in a long series of different medical specialties. Its non-invasive nature as well as the lack of use of ionizing radiation are now recognized advantages over other previously available imaging techniques, making magnetic resonance studies an integral part of the modern diagnostic armamentarium. Cardiology is no exception to this rule. Today, through the use of nuclear magnetic imaging, it is possible to obtain pictures with great anatomical detail of the heart, aorta

and other surrounding structures heretofore unavailable to conventional radiology and echocardiography. Magnetic resonance has also made possible to develop very sophisticated analyses of myocardial global and regional function such as myocardial tagging as well as the most precise so far determination of myocardial chamber volumes. Using similar technology and commercially available NMR scanners it is also possible to gain insight of metabolic processes and pathways with the application of nuclear magnetic resonance spectroscopy. All these techniques can be used to patients with heart failure of any cause and in particular to patients with Chagas' heart disease.

Chagas' heart disease is frequently associated with chronic myocarditis leading to heart failure, arrhythmias and sudden death (1,11). In experimental studies, cardiac magnetic resonance imaging (MRI) proved to be a sensitive modality to detect interstitial edema and myocardial infiltration with lymphocytes, including the

Address for correspondence:

Roberto Kalil Filho Instituto do Coração, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo Av. Dr. Enéas de Carvalho Aguiar, 44 São Paulo - SP - Brasil - CEP 05403-000 characterization of cardiac transplant rejection (4). Also, in previous clinical studies without the use of endomyocardial biopsy, magnetic resonance imaging has been used for the detection of acute myocarditis. One preliminary report suggested that magnetic resonance imaging could be useful for the diagnosis of myocarditis in infants and children and could be used as an attractive alternative method to endomyocardial biopsy for the non-invasive diagnosis of myocarditis in this age group (5).

However, these previous studies did not use gadolinium. In our opinion, the use of gadolinium is associated with a powerful enhancement for of the ability of magnetic resonance imaging to differentiate normal from inflamed tissue. Gadolinium is a paramagnetic contrast agent that marks areas with increased interstitial edema thus improving the ability of magnetic resonance imaging techniques to detect the presence of myocardial inflammatory processes. The use of this agent may explain in part the high sensitivity of MRI to detect inflammation in Chagas disease patients. In addition, preliminary data suggest that myocardial relaxation times and thus signal intensity are not changed in regions of myocardium in patients with cardiac dilatation per se (6), which would explain the unchanged signal intensity in our idiopathic dilated cardiomyopathy patients. Moreover, magnetic resonance imaging would appear to have certain advantages in the diagnosis of myocarditis in Chagas' disease, as it is not only non invasive but may also be more representative of the entire heart than a biopsy specimen.

The diagnosis of myocarditis in Chagas' heart disease has traditionally been based on the results of invasive endomyocardial biopsy or necropsy (2,9). Generally, the diagnosis of myocarditis is based on anatomopathological findings or endomyocardial biopsy results. Invasive right endomyocardial biopsy is the gold standard technique for the "in vivo" diagnosis of the myocardial inflammatory process in heart diseases in general, and of Chagas' heart disease in particular (7). However, the invasive nature of endomyocardial biopsy may bring recognized limitations such as morbidity, cost, possible complications, distress for sequential biopsies, and the potential for sampling error, which may cause low sensitivity when the inflammatory infiltrate is patchy or focal (10). Thus, there is a need for the development of non invasive techniques for the diagnosis of myocarditis. Magnetic resonance imaging has recently proved to be an emerging non invasive technique providing cardiac images with a high spatial resolution to depict cardiac anatomy and morphology(3). Increased signal intensity associated with interstitial edema and infiltration of the myocardium by lymphocytes have

been demonstrated in animal experiments. The tissue alterations caused by myocardial inflammation may induce abnormal signal intensity of the myocardial walls, which can be detectable in the clinical setting.

In a recent study, Bocchi et al. described the correlation between cardiac magnetic resonance, endomyocardial biopsy results, and Gallium-67 myocardial uptake for the non invasive diagnosis of myocarditis in Chagas' disease (3). Ten male patients with cardiomyopathy secondary to Chagas' disease, in congestive heart failure were studied. The patients were submitted to right ventricular endomyocardial biopsies, cardiac magnetic resonance imaging, and Gallium-67 myocardial uptake. The results of this group were compared with a control group of patients with idiopathic dilated cardiomyopathy. All patients with Chagas' heart disease showed higher signal intensity during magnetic resonance imaging after administration of gadolinium. According to the biopsy studies, eight Chagas' disease patients had evident signs of myocarditis and two other patients had borderline evidence myocarditis. In comparison, only one patient in the control group had a histologic diagnosis of borderline myocarditis, and no patient had evident myocarditis. Gallium-67 cardiac uptake was positive for myocardial inflammatory process in 7 Chagasic patients and borderline in one. On the other hand, only one patient in the control group had an uptake that was positive for inflammation and one had a borderline result. In conclusion, the data from this study strongly suggest that myocarditis is frequently found in Chagas' heart disease. Cardiac magnetic resonance imaging appears to be an accurate and alternative method for the diagnosis of inflammatory process associated with Chagas' heart disease.

Kalil et al. (8) used regional cardiac magnetic resonance imaging for the assessment of the inflammatory process in chronic Chagas heart disease. Cardiac signal intensity from the septal and free wall myocardial regions was compared with that from skeletal muscle before and after a bolus injection of gadolinium. Increased relative signal intensity was observed in the left ventricular free wall and in the septum (Figure 1). These findings showed that magnetic resonance imaging can non-invasively detect the presence and localization, as well as assess the heterogeneous nature of the distribution of the inflammatory process in Chagas's heart disease.

The development of imaging methods for the accurate assessment of abnormalities in the myocardium of patients with known or suspected Chagas' heart disease may have important therapeutic and prognostic consequences. Nuclear magnetic resonance can

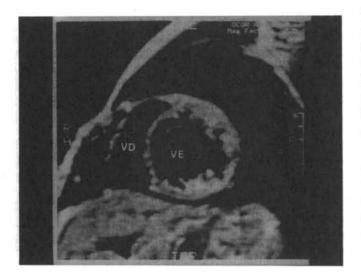


Figure 1. A typical example of a short axis nuclear magnetic imaging view of the heart at the level of the papillary muscles after the infusion of Gadolinium of a patient with Chagas' heart disease and biopsy proven significant myocarditis. Note the greater signal intensity of the lateral and posterior walls of the left ventricle.

demonstrate Chagas' heart disease myocarditis noninvasively. Also, the results of Bocchi's study show that magnetic resonance imaging may be an attractive method for diagnosis of myocardial inflammatory process in chronic Chagas' heart disease with a favorable performance when compared with endomyocardial biopsy results and Gallium-67 cardiac uptake.

The high incidence of myocarditis in Chagas' disease patients is in accordance with other publications which showed that the presence and persistence of myocardial damage by inflammatory process are common morphological findings in chronic chagasic cardiomyopathy (7,10). It has been shown that there is a high prevalence of diffuse or focal chronic inflammatory process, diffuse interstitial fibrosis, degeneration and hypertrophy of cardiac fiber in chronic Chagas' heart disease (9).

Kalil et al. and Bocchi et al. reported still preliminary studies with small number of patients (3,8). However, their results are noteworthy. The gold standard for validation of the magnetic resonance imaging technique or for any other method used for the diagnosis and distribution of myocarditis should be the realization of multiple biopsies in many segments of the heart or a post-mortem pathological examination of the whole heart, which was clearly not possible. The association of endomyocardial biopsy, Gallium-67 myocardial uptake and magnetic resonance imaging in this study is an alternative to improve the analysis of the role of each method.

In summary, magnetic resonance imaging seems to be a good diagnostic method to detect myocarditis in chronic Chagas' heart disease. Its use in the diagnosis of chronic Chagas' heart disease myocarditis is promising and it has the potential to be a useful alternative to endomyocardial biopsy. An important advantage of magnetic resonance imaging is the ease of performance of serial studies as may be necessary in long-term follow-up. Further observations on larger number of patients will be of interest to confirm these results and determine the sensitivity and specificity of magnetic resonance in the detection of myocarditis in chronic Chagas' heart disease and define its realistic clinical role.

RESUMO

Muitos aspectos importantes na doença de Chagas podem ser avaliados utilizando-se a imagem cardíaca gerada por ressonância nuclear magnética. É possível obter a caracterização anatômica das câmaras cardíacas em detalhes e também importantes informações do estado funcional e metabólico do coração. A imagem por ressonância nuclear magnética após infusão de gadolíneo parece ser uma técnica promissora para obter uma melhor caracterização regional do tecido miocárdico, e pode ser importante no diagnóstico não invasivo da miocardite ativa em pacientes com doença de Chagas.

REFERENCES:

- ACOSTA, A.M. & SANTOS-BUCH, C.A. Autoimmune myocarditis induced by *Trypanosoma cruzi*. Circulation 6:1255-61, 1985.
- BARRETO, A.C.P.; MADY, C.; ARTEAGA-FERNANDES, E.; STOLF, N.; LOPES, E.A.; HIGUSHI, M.L. et al. - Right ventricular endomyocardial biopsy in chronic Chagas' disease. Am Heart J 111: 307-312, 1986.
- BOCCHI, E.; KALIL, R.; ROSEMBERG, L.; MAGALHÃES, A.; ANTELMI, I.; MADY, C. et al - Magnetic resonance imaging in Chagas Disease: Correlation with endomiocardial biopsy. Circulation 88: I-536 (abstract), 1993.
- EDELMAN, R.R. & WARACH, S. Magnetic resonance imaging. N Engl J Med 328: 708-716, 1993.
- GAGLIARI, M.G.; BEVILACQUA, M.; RENZI, P.; SEGURO, R.; PASSARELLO, R. & MARCELLETTI, C. -Usefulness of magnetic resonance imaging for diagnosis of acute myocarditis in infants and children, and comparison with endomyocardial biopsy. Am J Cardiol 68:1089-1091, 1991.
- GELTMAN, E.M.; EISENBERG, J.D.; KEIM, S.; ATKINSON, D.; SOBEL, B.E. & LEVITT, R.G. -Comparative magnetic resonance imaging and positron

- emission tomography in cardiomyopathy. **J Am Coll Cardiol** 5:436 (abstract), 1985.
- HIGUCHI, M.L.; MORAIS, C.F.; PEREIRA-BARRETO, A.C.; LOPES, E.A.; STOLF, N.; BELLOTTI, G. et al. - The role of active myocarditis in the development of heart failure in chronic Chagas' disease: a study based on endomyocardial biopsies. Clin Cardiol 10:665-670, 1987.
- KALIL FILHO, R.; WEISS, R.; ROSEMBERG, L.; BOCCHI, A.E.; MAGALHÃES, C.A.; BACAU, F. et al. -Regional cardiac magnetic resonance imaging for the assessment of inflamatory progress in chronic heart disease. J Am Coll Cardiol 23:150A (abstract), 1994.
- LARANJA, F.S.; DIAS, E. & NÓBREGA, G. Chagas' heart disease: a clinical, epidemiologic and pathologic study. Circulation 14:1035-60, 1956.
- MILEI, J.; STORINO, R.; ALONSO, G.F.; BEIGELMAN, R.; VANZULLA, S. & FERRANS, V. - Endomyocardial biopsies in chronic chagasic cardiomyopathy. Cardiology 80: 424-437, 1992.
- RAHIMTOOLA, S.H. & HAGA, J.M. Chagas' heart disease in the United States. N Engl J Med 325:763-8, 1991.