Revista Brasileira de Cirurgia Cardiovascular/Brazilian Journal of Cardiovascular Surgery
ISSN: 0102-7638
bjcvs@sbccv.org.br
Sociedade Brasileira de Cirurgia Cardiovascular

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Cardiac resynchronization therapy for patients with chronic systolic heart failure secondary to Chagas cardiomyopathy in the 21 st century
Revista Brasileira de Cirurgia Cardiovascular/Brazilian Journal of Cardiovascular Surgery, vol. 29, núm. 1, enero-marzo, 2014, pp. IV-VI
Sociedade Brasileira de Cirurgia Cardiovascular
São José do Rio Preto, Brasil

Cardiac resynchronization therapy for patients with chronic systolic heart failure secondary to Chagas cardiomyopathy in the 21st century

Terapia de ressincronização cardíaca em pacientes com insuficiência cardíaca crônica sistólica secundária à cardiomiopatia da doença de Chagas no século 21

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DOI: 10.5935/1678-9741.20140002

In the 21st century, Chagas disease continues to be a major health problem in South America because it affects 10 million people, and other 20 million are at risk of acquiring the disease [1]. It must be emphasized, however, that the disease is no longer confined to South America due to international immigration. In fact, Chagas disease has persistently been identified in non-endemic countries such United States, Spain, Canada, and Australia [1]. As a result, the global economic burden of the disease is impressive, reaching the figure of US 8 billion annually [2].

Chagas disease is caused by the protozoan *Trypanosoma cruzi*, which is transmitted to humans when the feces of a sucking bug contaminate a skin lesion or eye mucosae [1]. However, chronic Chagas disease appears many years after initial infection (in general, up two decades). Chagas cardiomyopathy is the protean clinical manifestation of the chronic disease, manifesting by ventricular dysrhythmias [3], sudden cardiac death [4], thromboembolism [5], and chronic heart failure (CHF) [6].

In Chagas disease patients, CHF is associated with reduced systolic function, as no case of CHF with preserved left ventricular function has been described in patients with this condition. The disease can affect up to 5% of patients of a population-based and about 50% of a referral center-based cohort [6]. Chagas disease heart failure has a higher annual mortality [7], and its prognosis is worse than that observed in non-Chagas disease heart failure [8]. Irreversible left ventricular systolic dysfunction is the most frequent mode of death in patients with this condition in the contemporary era [9].

The pathogenesis of Chagas disease heart failure is similar to that seen in non-Chagas disease heart failure, with the neurohormonal activation playing a pivotal role. In addition, an intracardiac autonomic imbalance [10] can expose the myocardium to the toxic effects of catecholamine [11]. Some studies suggest a benefit effect for angiotensin converting enzyme inhibitor as well as for beta-blocker therapy both experimentally [12] and in patients with this condition [8,13,14]. Obviously, other types of treatment modality are necessary, mainly in patients in the advanced stages of CHF.

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Cardiac resynchronization therapy (CRT) is an established therapeutic modality for patients with non-Chagas heart disease heart failure to improve mortality in those with advanced heart failure and left bundle branch block [15,16]. In a Brazilian scenario, this therapy is also cost-effective [17]. By contrast, little is known about the effects of CRT in patients with CHF secondary to Chagas cardiomyopathy in view of the few studies carried out in patients with this condition. Silva Menezes [18] has clearly shown that CRT with bifocal right ventricular pacing has no effect on left ventricular reverse remodeling in the mid-term follow up, besides increasing the number of arrhythmic episodes. Silva et al. [19] studied 29 patients with CHF, 52% of them with CHF secondary to Chagas cardiomyopathy with permanent right ventricular pacing. They showed in this small sample that CRT improves clinical status and left ventricular ejection fraction in the mid-term follow up in patients with Chagas disease heart failure, although a definite conclusion could not be established because such a study was neither randomized nor double-blinded. Therefore, further studies on the effect of CRT on patients with CHF sec-

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Abbreviations, acronyms & symbols	
CHF	Chronic heart failure
CRT	Cardiac resynchronization therapy

ondary to Chagas cardiomyopathy are sorely needed if we are planning to improve morbidity and mortality in such patients.

In this issue of the journal, Araújo et al. [20] presents a paper dealing with CRT in patients with CHF secondary to Chagas cardiomyopathy. The authors enrolled 72 patients in class III/IV, 100% on beta-blocker therapy (mean carvedilol daily dose=20 mg), 70% on angiotensin converting enzyme inhibitor/angiotensin receptor block, 47% with left bundle branch block, mean QRS duration 148.1 ± 17.5 msec, 15% on permanent right ventricular pacing, mean left ventricular systolic diameter 66.2 ± 7.6 mm, and mean left ventricular ejection fraction 27.3 ± 7.7%. After a mean follow-up of 47 months, only 13% were in class III/IV, there was an 81% increase in the left ventricular ejection fraction, and a 12% decrease in the left ventricular systolic diameter. Importantly, this is the largest cohort of patients with CHF secondary to Chagas cardiomyopathy receiving CRT thus far reported. Araújo et al [20], therefore, did observe left ventricular reverse remodeling in such patients. However, it must be emphasized that such a study was neither randomized nor double-blinded.

In the absence of evidence-based medicine support, it could be difficult to recommend CRT to treat patients with Chagas cardiomyopathy with CHF. Of course, a randomized, double-blinded controlled trial would be paramount to recommend or not to recommend CRT to Chagas disease patients. However, it should be borne out that Chagas disease is neglected, and therefore such a study will probably never be carried out in patients with this disease. Therefore, in a scenario like that, it seems to me to be reasonable to indicate CRT to patients with CHF secondary to Chagas cardiomyopathy with a clinical picture similar to that found in non-Chagas disease heart failure patients. This is an important question because even patients with non-Chagas disease heart failure have different types of heart disease, but have been treated similarly. This is the case, for example, for patients with CHF secondary to either idiopathic dilated cardiomyopathy or ischemic cardiomyopathy, which are distinct entities.

With the limitations discussed earlier, the paper by Araújo et al. [20] may be seen as another block in the construction of the treatment of patients with CHF secondary to Chagas cardiomyopathy in the contemporary era. Furthermore, Araújo et al. paper lends support to the notion that such patients, treated with guideline drugs (at target doses) [21], with increased QRS complex duration (ideally with left bundle branch block), and advanced left ventricular remodeling (as detected by left ventricular ejection fraction < 30% and left ventricular systolic dimension > 50 mm), will benefit of CRT.

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