

Parasympathetic Impairment in the Preclinical Stage of Chronic Chagas Disease

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Dear Editor,

We have read with great interest the paper by Vasconcelos and Junqueira-Júnior¹ who showed that parasympathetic and sympathetic abnormalities occur in patients with chronic Chagas heart disease with no left ventricular systolic dysfunction. These abnormalities were observed in heart rate variability in the time and frequency domain. They concluded that "it is improbable that the marked cardiac autonomic dysfunction can merely be a phenomenon secondary to slight ventricular mechanic disturbance". We agree.

We have demonstrated that only parasympathetic impairment can be observed in heart rate variability in the frequency domain of patients with chronic Chagas disease with no left ventricular systolic dysfunction². We studied 97 patients, the left ventricular ejection fraction being similar in patients with and in those without parasympathetic impairment. Nonetheless, 8 (8%) of 97 patients with no electrocardiographic abnormality in the 12-lead electrocardiogram and no left ventricular systolic dysfunction at echocardiography had parasympathetic impairment. By contrast, sympathetic derangement was not observed in any of the patients with normal 12-lead electrocardiogram and echocardiogram. However, in patients with chronic Chagas heart disease, as

observed in the study by Vasconcelos e Junqueira-Júnior, the proportion of sympathetic and parasympathetic dysfunction was similar to that found in our study.

The fact that isolated parasympathetic impairment can be observed in patients with chronic Chagas disease at the preclinical stage may suggest a role for parasympathetic derangement in the pathogenesis of chronic Chagas heart disease. In fact, parasympathetic damage has been shown to induce chronic cardiomyopathy experimentally³. Therefore, independently of the presence of sympathetic derangement at the preclinical stage, as shown by Vasconcelos and Junqueira-Júnior, the precocious parasympathetic withdrawal in the clinical course of Chagas disease, with the consequent increase in myocardial tumor necrosis factor, microvascular spasm, platelet aggregation, and myocardial necrosis/ischemia may play a causative role in the pathogenesis of Chagas heart disease.

The presence of early parasympathetic impairment can also account for the beneficial effects of Beta-Blocker therapy, experimentally⁴ and in patients with Chagas heart disease⁵. Thus, we think that the data provided by Vasconcelos and Junqueira-Júnior reinforce the notion that autonomic dysfunction is a primary phenomenon and should no more be seen as a secondary phenomenon to left ventricular systolic dysfunction.

We suggest that a longitudinal prospective cohort study is mandatory to evaluate whether parasympathetic impairment, as detected by heart rate variability in the frequency domain, has a causal relationship with the appearance of cardiomyopathy in patients with chronic Chagas disease.

Keywords

Chagas Cardiomyopathy;/physiopathology; Heart Rate/physiology; Autonomic Nervous System.

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Response Letter

We appreciate the interest of Gerbi et al.¹ in reading our article and thank them for their contribution with complementary comments based on data they recently published¹. These data reinforce our findings that the cardiac autonomic dysfunction in Chagas' disease appears to be a primary phenomenon of varying intensity without a strict relation of cause and effect to the progressive contractile disturbance².

In the early studies on Chagas heart disease, the autonomic disturbances were already considered to be the cause of the progressive mechanical alterations of the heart. Similar to the mechanism of the digestive disease, where the parasympathetic denervation was proved to be the cause of the dilatation of the esophagus and segments of the intestine, the parasympathetic depression associated with a relative increase of the sympathetic activity would be the determinant of the hypertrophy and dilatation of the heart³. This concept, however, was not corroborated by many subsequent studies, whose authors concluded that the progressive contractile alteration of the heart critically depends on the underlying evolutionary chronic fibrotic inflammation of the myocardium^{4,5}. Therefore, the autonomic denervation and consequent disturbance of the cardiac neural control do not seem to be a direct cause of the contractile dysfunction^{2,6-10}.

Studies with ¹²³I-metaiodobenzylguanidine to evaluate the sympathetic innervation^{11,12} and with ²⁰¹thallium to evaluate the myocardial perfusion, detected an association between sympathetic denervation and reduced perfusion and segmental systolic dysfunction, in chagasics without evidence of cardiac involvement by conventional methods, suggesting that the sympathetic dysfunction could precede the contractile alteration.

In a correlative functional study in chagasic subjects, we observed that the contractile, electrical and autonomic disturbances, as detected by means of echocardiography, conventional electrocardiogram and Valsalva maneuver, respectively, occurred alone or in combination in any of the clinical forms of the disease. Otherwise, some chagasics did not show evidence of any of these disturbances¹³. These findings suggest that the functional disturbances of the heart are not necessarily related to one another on the basis of a causal relationship.

In other words, the autonomic impairment, especially the parasympathetic impairment, can occur alone without contractile alteration, in association with this alteration, or even be absent in the presence or absence of the mechanical disturbance. These alternatives of relationship between the two cardiac functions are observed particularly in the cardiac form of the disease. In the indeterminate or preclinical form, these alternatives are more elusive because ostensive manifestations of cardiac disease cannot be detected. Therefore, the relationship between the autonomic and contractile dysfunctions cannot be established in terms of cause and effect in one or other direction¹⁰. This concept is reinforced by other studies demonstrating that the cardiac autonomic dysfunction is a precocious and independent phenomenon of the contractile alteration^{2,7,14,15}, including the recent work by Gerbi et al., which also detected no relationship between both disturbances using also heart rate variability analysis to characterize the autonomic status¹.

However, when both disturbances are simultaneously present, possibly the autonomic dysfunction can influence the contractile dysfunction, considering the relevant regulatory action of the autonomic nervous system on the myocardial function, but not as a relationship of causal basis. Indeed, it is physiologically logical to consider that the autonomic nervous system as a functional controller should exert an effect on the myocardial function as a controlled structure. It is only in the situation of cardiac failure that the autonomic dysfunction commonly and secondarily results from this syndrome, in the context of its pathophysiology.

Finally, despite these several convincing observations, we agree that well-controlled longitudinal prospective studies should be further carried out in order to clarify the relationship between the autonomic and contractile disturbances in the course of Chagas disease¹⁰. However, in our environment, conducting such studies is a very difficult task. Perhaps, the best way is to conduct them in a supervised endemic area of Chagas disease, where the subjects can be followed up for a long time.

Sincerely,

Daniel Franca Vasconcelos

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Letter to the Editor

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