

Functional capacity in Chagas disease

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Chagas disease remains an important health problem worldwide, with more than 6 million persons infected in Latin American endemic countries and hundreds of thousands of infected immigrants living in Europe and North America¹. In Brazil, although its prevalence is declining, the Global Burden of Disease Project estimated 5,952 (range, 5,498-6,453) deaths due to Chagas disease in 2015². In 2016, among all neglected tropical diseases in Brazil, Chagas disease was the leading cause of DALYs - disability-adjusted life-years [141,640; 95% confidence interval (95% CI), 129,065-155,941], a measure of health loss due to fatal and non-fatal disease burden³. Chagas disease is a paradigmatic example of a neglected tropical disease, a group of preventable, stigmatizing, disabling, debilitating, and potentially lethal communicable diseases that predominantly affect the poor and vulnerable populations of the developing world⁴. The meaning of *neglected* for Chagas disease is wide and deep, and the disease has been forgotten in many different ways. Chagas disease is not always mentioned as the underlying cause of a patient's death, leading to underreporting of the number of deaths attributable to it⁵. Clinical trials of Chagas disease, both for specific and syndromic treatment, are scarce, and the current management of Chagas cardiomyopathy relies largely on recommendations transposed from guidelines developed for other cardiopathies⁶. There is also a need for comprehensive data on the clinical presentation and natural history of the disease.

In this issue, Costa et al.⁷ presented a study that contributes to our understanding of an important feature in Chagas disease, i.e., the existence (or not) of reduced functional capacity in different stages of the disease. Patients with dilated Chagas heart disease (CHD) undoubtedly have impaired functional capacity, but consensus is lacking about whether patients without apparent cardiopathy or with non-dilated CHD are similarly affected⁷. To answer this question, the authors performed a systematic review of studies that evaluated the measured or estimated peak oxygen consumption (VO₂ peak) in Chagas disease patients classified in at least one of these stages compared to that in a control group.

The results were summarized and meta-analyzed to compare VO₂ peak between healthy subjects and patients with Chagas disease without apparent cardiopathy, non-dilated CHD, and dilated CHD.

From 363 studies obtained using a standard strategy in several databases, only seven fulfilled the selection criteria and were included in the review. Six of these studies assessed functional capacity using a treadmill, and four of seven measured VO₂ peak directly. Study quality was assessed by using the Newcastle-Ottawa scale, and random effects models were used when moderate to high heterogeneity was present. Chagas disease patients without cardiopathy (n = 208) had VO₂ peak values similar to those of healthy controls (n = 105), but those with non-dilated CHD (n = 159) had significantly lower VO₂ peak values than healthy controls (difference: 8.71, 95% CI, 13.99-3.42mL/kg/min) with high heterogeneity (I², 75%). Those with dilated CHD (n = 131) had reduced VO₂ peak values compared to healthy controls without heterogeneity in the meta-analysis.

The interpretation of these results should consider the small number of studies retrieved by the authors and the uncertainty introduced by the high heterogeneity and large 95% confidence interval observed in the meta-analytic comparison of patients with non-dilated CHD and healthy subjects, limitations acknowledged by the authors. Different studies may also have used slightly different stage definitions since there is a wide spectrum of clinical and pathological manifestations in Chagas disease patients^{1,6}, leading to different profiles of patients included in the groups compared by the meta-analysis. However, it is important to understand why such patients without overt left ventricular systolic dysfunction seemed to have reduced capacity to exercise. One putative explanation is the presence of chronotropic incompetence observed in non-dilated CHD patients, which is related to both reduced vagal heart variability indexes and reduced exercise duration and estimated VO₂ peak^{8,9}. Vagal heart dysfunction can occur even in Chagas disease patients without apparent cardiopathy¹⁰, but it worsens as the left ventricular function deteriorates with disease progression¹¹ and may affect exercise ability in patients with non-dilated CHD. Other mechanisms can be related to diastolic dysfunction, which can occur in early Chagas disease patients without apparent cardiopathy and is more intense in those with

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non-dilated CHD¹². Functional capacity assessed by VO₂ peak is related to increased left ventricular (LV) filling pressures and diastolic dysfunction independent of systolic function in patients with Chagas cardiomyopathy¹³. Right ventricular (RV) function, an important factor in functional capacity¹⁴, may be compromised in the early stages of Chagas disease¹⁵. Ventricular arrhythmias, a hallmark of CHD that is common in non-dilated patients¹⁶, may also be induced by exercise and impair an individual's ability to reach maximal effort. The existence of so many possible mechanisms to explain the reduced functional capacity in the early stages of CHD suggests that this phenomenon may be multifactorial and vary among patients, a feature that is compatible with the pleomorphic clinical presentation of the disease.

All of these findings stress the importance of the present study and identify the need for further studies to determine the reduction in exercise capacity in the early stages of Chagas disease and evaluate the role of exercise training in its treatment. As the authors observed, small studies have demonstrated the benefit of physical rehabilitation in the general well-being, functional capacity, autonomic heart control, respiratory muscle strength, and quality of life of CHD patients¹⁷⁻²⁰. Larger studies on the implementation and cost-effectiveness of this much-valued therapeutic approach are welcome and can contribute to the general goal of improving quality of life in patients with this highly neglected tropical disease.

Conflict of interest

The author declares that there is no conflict of interest.

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