

Maximal Functional Capacity, Ejection Fraction, and Functional Class in Chagas Cardiomyopathy. Are these Indices Related?

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Objective

Left ventricular ejection fraction (LVEF) and maximal functional capacity (VO_2max) have both been shown to be related to a poor long-term survival in Chagas' disease patients. The aim of this study was to estimate the potential association of VO_2max , LVEF, and NYHA functional class in patients with Chagas' disease cardiomyopathy.

Methods

One hundred four male patients, aged 40.3 ± 9.0 years (range, 18 to 65), with a definite diagnosis of Chagas disease cardiomyopathy were studied. LVEF and VO_2max were both classified into 3 degrees: $LVEF \leq 0.30$, $0.30 < LVEF \leq 0.50$, and $LVEF > 0.50$ and $VO_2max \leq 10$, $10 < VO_2max \leq 20$, and $VO_2max > 20 \text{ ml.kg}^{-1}.\text{min}^{-1}$, respectively.

Results

Thirty-one patients (29.8%) were in NYHA functional class II, 41 (39.4%) in functional class III, and 32 (30.8%) in functional class IV. The corresponding values of VO_2max and LVEF for functional classes II, III, and IV were $21.5 \pm 4.0 \text{ ml.kg}^{-1}.\text{min}^{-1}$, $18.3 \pm 5.8 \text{ ml.kg}^{-1}.\text{min}^{-1}$, and $14.7 \pm 4.9 \text{ ml.kg}^{-1}.\text{min}^{-1}$ and 0.50 ± 0.6 , 0.35 ± 0.9 , and 0.29 ± 0.7 , respectively. $LVEF = \leq 0.30$ and $VO_2max = \leq 10 \text{ ml.kg}^{-1}.\text{min}^{-1}$ were found in the majority of patients in NYHA functional class IV. Conversely, patients in functional class II were mostly those with $LVEF > 0.50$ as well as $VO_2max > 20 \text{ ml.kg}^{-1}.\text{min}^{-1}$.

Conclusions

A convincingly good association exists between NYHA functional class, functional capacity and LVEF in patients with Chagas' disease cardiomyopathy. These data may be helpful in the management of heart failure in Chagas' disease patients.

Key words

maximal functional capacity, ejection fraction, functional class in Chagas cardiomyopathy

Chagas' disease is an infectious disease caused by the protozoan *Trypanosoma cruzi*, which may result in a dilated form of cardiomyopathy, usually complicated by congestive heart failure¹. The extent of myocardial involvement and its functional consequences are the fundamental determinants of the natural history^{2,3}. Similarly to that in other forms of heart failure⁴⁻⁷, mortality increases as myocardial function deteriorates³. In addition, left ventricular ejection fraction (LVEF) and maximal functional capacity (VO_2max) have both been shown to be related to a poor long-term survival in Chagas' disease patients³.

Surprisingly, however, some studies on other forms of dilated cardiomyopathy have demonstrated that, despite having a severe left ventricular impairment, a rather normal functional capacity may be found^{8,9}. In addition, some reports show a lack of connection between LVEF and VO_2max in these patients¹⁰⁻¹³. These findings indicate that the traditional indices widely used for the evaluation of cardiac function and functional capacity are not entirely appropriate for all patients with heart failure. Contrasting with these reports, it has been previously shown in patients with Chagas' cardiomyopathy that VO_2max progressively worsens as left ventricular chamber dimension increases^{14,15}.

Therefore, in view of these conflicting data, the aim of the present study was to investigate the potential association of VO_2max and LVEF with functional class in Chagas' disease.

Methods

All procedures were carried out in accordance with institutional guidelines, and the protocol was approved by our institutional review committee. Before entering the study, patients underwent complete clinical and biochemical evaluations. Those with a suggestive history of ischemic heart disease, valvular heart disease, diabetes, alcohol abuse, renal failure (serum creatinine $> 1.4 \text{ mg/dL}$), anemia (serum hemoglobin $< 12 \text{ g/L}$), and systemic hypertension were excluded from the study. The diagnosis of Chagas' disease was suggested by positive epidemiological evidence, clinical history, and physical and laboratory findings indicating a dilated form of cardiomyopathy concurrently with typical ECG changes¹⁶ and ultimately confirmed by specific serological tests (Machado-Guerrero and immunofluorescence).

One hundred four male patients aged 40.3 ± 9.0 years (range, 18 to 65) with congestive heart failure due to Chagas' cardiomyopathy were selected and gave informed consent to enter the study. All patients were admitted to the hospital and received

traditional measures aimed at heart failure treatment, which included bed rest, digitalis, diuretics, and vasodilator drugs, including angiotensin-converting enzyme inhibitors. Heart failure status was classified at the time of entering the study according to the criteria established by the New York Heart Association (NYHA) ¹⁷.

All patients after having been stabilized for heart failure symptoms underwent ergospirometry for $VO_2\text{max}$ ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) determination using a Metabolic Cart (MGC CAD/NET 1988, Minneapolis, MN, USA). Respiratory variables were obtained under conditions of standard temperature, pressure, and humidity (StPD) with appropriate correction factors being used. All patients underwent a maximal exercise test based on the modified Naughton protocol ¹⁸ using monitoring treadmill equipment (Quinton, model Q65, Seattle, Washington) with variable speed and inclination.

We used conventional echocardiographic equipment. The echocardiographic parameters were determined, based on the recommendations of the American Society of Echocardiography ¹⁹.

Maximal functional capacity and cardiac function were categorized as follows: $VO_2\text{max} \leq 10$, $10 < VO_2\text{max} \leq 20$, $VO_2\text{max} > 20$ $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, and $LVEF \leq 0.30$, $0.30 < LVEF \leq 0.50$, $LVEF > 0.50$, respectively.

Patients stratified according to functional class were compared regarding $VO_2\text{max}$ and LVEF by using the analysis of variance and the Duncan's multiple comparison method ²⁰.

The potential associations of NYHA functional class with $VO_2\text{max}$ and LVEF were tested using the analysis of correspondence²¹, which is a multivariate exploratory method of categorical data for converting a contingency table into a 2-dimensional chart. In this chart, a distinctive vector for each category represents each one of the 3 variables studied. The potential association of a pair of categories studied is expressed by a small angle between their corresponding vectors.

All statistical calculations were performed using SAS software (Statistical Analysis System). The significance level was established at 0.05. Continuous variables are expressed as mean value \pm SD.

Results

Thirty-one patients aged 41.0 ± 7.9 years were in NYHA functional class II, 41 patients aged 41.2 ± 8.6 years were in functional class III, and 32 patients aged 39.8 ± 8.1 years were in functional class IV. LVEF and $VO_2\text{max}$ values according to patient's functional class are depicted in table I. As can be observed, each one of the 3 categories of heart failure studied showed statistically different LVEF and $VO_2\text{max}$.

Figure 1 shows the chart representing the results of the analysis of correspondence. We can observe that the variables LVEF and $VO_2\text{max}$ were both associated with NYHA functional class. As a matter of fact, the vectors corresponding to $LVEF > 0.50$, $VO_2\text{max} > 20$ $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, and functional class II are within the same quadrant, and the angles between each 2 of them are all small. A similar association is evident for the following 2 groups of categories analyzed: $0.30 < LVEF \leq 0.50$, $10 < VO_2\text{max} \leq 20$ $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and functional class III; and $LVEF \leq 0.30$, $VO_2\text{max} < 10$ $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, and functional class IV.

In short, the results of this analysis are in agreement with that of the analysis of variance showing an evident association of

functional class, LVEF, and $VO_2\text{max}$, indicating that the more advanced the functional class, the more impaired both functional capacity and cardiac function are.

Discussion

In general, it is agreed that functional exercise capacity is significantly related to the severity of heart failure. This represents the basis of the universally adopted subjective clinical classification of heart failure recommended by the New York Heart Association¹⁷. This observation is based on the well-documented relationship found between functional capacity and cardiac performance, manifested by a positive correlation between $VO_2\text{max}$ and cardiac output ^{22,23}. However, some investigators were unable to demonstrate such a relationship between LVEF and $VO_2\text{max}$ ¹⁰⁻¹³. Moreover, exercise capacity was found to be quite normal in a significant number of patients with severe left ventricular dysfunction ^{8,9}. Therefore, the premise that functional exercise capacity represents a good index for evaluating and predicting cardiac performance has been questioned. We speculate that these contradictory findings are the result of improperly classifying cardiac function merely as normal or abnormal in some of these studies. To avoid such a shortcoming, in the present study patients were classified according to 3 different categories of LVEF and maximal exercise capacity. Accordingly, the 37 patients with $VO_2\text{max}$ values over 20 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ were actually those who were the least symptomatic and with the highest values of LVEF.

Currently, data concerning functional exercise capacity and cardiac function provide the essential information for making confident clinical and surgical therapeutic decisions in patients with heart failure. Recently, it has been shown that clinical history alone is far from being a reliable method for determining functional capacity in patients with ischemic heart disease and other forms of cardiomyopathy ²⁴. The heterogeneity of the population studied might have represented an important drawback in that investigation. It has long been recognized, for instance, that survival curves may differ according to the underlying cause of heart disease ²⁵. It is also well known that men compared with women with equivalent heart failure status show a higher exercise capacity ²⁶. In the present study, only male patients, all with Chagas' cardiomyopathy, were included. However, a previous study showed that in male patients individuals with Chagas' disease were at higher risk of progression of the disease, defined as death or the presence of a new ECG or left ventricular echocardiographic abnormality on follow-up, making these patients a subgroup with increasing risk of adverse events ²⁷.

The association between the impairment of $VO_2\text{max}$ and poor long-term prognosis has been debated ^{28,29}. A strikingly limited short-term survival has been demonstrated in patients with a marked exercise limitation, corresponding to a $VO_2\text{max}$ below 10 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ²⁸. When patients with such a degree of exercise capacity impairment are excluded from the analysis, exercise capacity provides little prognostic information ²⁹. In contrast, it has been previously demonstrated that $VO_2\text{max}$ is in fact a good predictor of survival in patients with heart failure due to Chagas' disease ³. The prognostic significance of $VO_2\text{max}$ remained strong even if Chagas' disease patients with only mild left ventricular dysfunction were included. In accordance with our findings, a



Table 1 - Comparison of left ventricular ejection fraction (LVEF) and maximal functional capacity (VO₂max) among the three different groups of NYHA functional class

NYHA Functional class	LVEF	p	Duncan's multiple comparison	VO ₂ max	p	Duncan's multiple comparison
II	48.21±6.61	0.0001	*	21.48±4.05	0.0001	*
III	35.34±9.29	0.0001	†	18.30±5.80	0.0001	†
IV	29.09±6.76	0.0001	‡	14.70±4.89	0.0001	‡

Groups with different symbols (*, †, ‡) are statistically different.

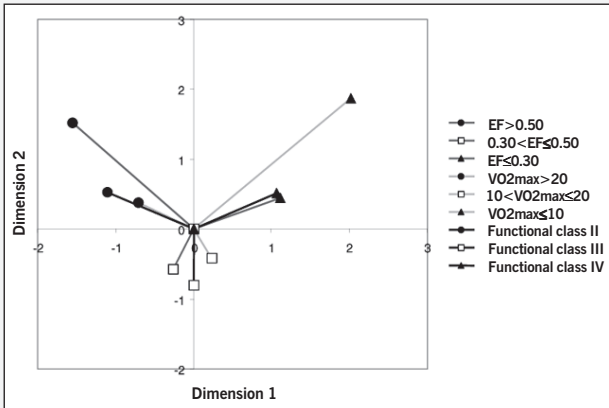


Fig. 1 - Two-dimensional graphic representation of the association found among NYHA functional class, left ventricular ejection fraction (LVEF), and maximal exercise functional capacity (VO₂max.).

previous study showed that the functional capacity of patients in the initial phase of chronic Chagas' disease is higher than that of patients in an advanced phase, and that this functional capacity decreases following the myocardial functional impairment³⁰.

LVEF is also recognized as a valuable index for estimating outcome in patients with heart failure³¹. Yet again, as previously pointed out for both functional class and exercise capacity, conflicting data exist regarding the ability of LVEF in predicting survival.

Although LVEF has been reported not to differ between survivors and nonsurvivors³², a significant and positive relation between LVEF and long-term survival has been documented^{33,34}. Once again, it became apparent from previous reported data that LVEF might have in fact a marked influence on survival of patients with heart failure due to Chagas' cardiomyopathy³. The present results, demonstrating a significant association of LVEF with both functional class and exercise capacity, underscores one of the major mechanisms involved in the predictive value of LVEF on survival, namely impairment in functional capacity.

In the present study, we were able to demonstrate that NYHA functional class is related to functional exercise capacity and cardiac function in patients with Chagas' cardiomyopathy. Accordingly, the more advanced the functional class, the more severely both exercise capacity and cardiac performance are affected. Based on these results, we may, thus, infer that the traditional indices currently used for clinical evaluation of patients with heart failure are very consistent for patients with Chagas' disease.

We are convinced that these data will be helpful in the management of heart failure in the setting of Chagas' disease. The consistency of the traditional indices used for cardiac evaluation herein demonstrated certainly will help making more appropriate therapeutic decisions for each individual patient, taking into account, firstly, the severity of the disease and, ultimately, bearing in mind the new modalities of treatment.

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