

# Relation Between Left Atrial Dimension and Exercise Capacity in Endomyocardial Fibrosis

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## Objective

To assess whether exercise capacity is related to left atrial dimension (LAD) in patients with biventricular endomyocardial fibrosis.

## Methods

This study comprised 38 patients in sinus rhythm, with a mean age of  $37.5 \pm 11.5$  years (range, 11 to 59 years), 25 of whom were women. They were divided into 2 groups according to the NYHA functional class on hospital admission as follows: group A (12 patients) and group B (26 patients). All patients underwent cardiopulmonary exercise testing to determine their maximum oxygen consumption ( $VO_2$  max), and their left atrial dimension was determined on echocardiography.

## Results

The  $VO_2$  max values for groups A and B were  $21.8 \pm 4.8$  mL.kg<sup>-1</sup>.min<sup>-1</sup> and  $13.7 \pm 3.5$  mL.kg<sup>-1</sup>.min<sup>-1</sup>, respectively, and the left atrial dimensions were  $3.7 \pm 0.7$  cm and  $4.4 \pm 0.7$  cm for groups A and B, respectively. A significant and inverse correlation was found between  $VO_2$  max and LAD in the groups studied.

## Conclusion

The increase in left atrial dimension is associated with impairment in exercise capacity in patients with endomyocardial fibrosis. Our findings support the use of left atrial dimension to estimate a more complex and difficult to assess index of functional capacity, such as  $VO_2$  max.

## Key words

left atrial dimension, exercise capacity, endomyocardial fibrosis

Endomyocardial fibrosis (EMF) is a rare restrictive cardiomyopathy characterized by fibrous thickening of the endocardium and adjacent myocardium. The apex and ventricular inlet are most commonly involved, which often results in obliteration of one or both ventricular cavities<sup>1</sup>. Usually, the build-up of fibrous tissue extends to the papillary muscles interfering with the anatomy and function of the atrioventricular valvular apparatus. The morphological alterations in the ventricular chambers added to the atrioventricular valvular dysfunction cause a restrictive syndrome, which usually manifests as bilateral, or mainly right ventricular, diastolic heart failure<sup>2-6</sup>. One of the most important pathophysiological adaptive mechanism is atrial enlargement<sup>1,5</sup>, which seems to play a fundamental role in maintaining cardiac output. Exercise intolerance, assessed through cardiopulmonary exercise testing, is a fundamental determinant of clinical evolution in patients with heart failure<sup>7,8</sup> and reflects much more the alterations in left ventricular diastolic function than in systolic function<sup>9</sup>. However, cardiopulmonary exercise testing is of limited clinical application in those patients, because most of them have signs and symptoms of advanced heart failure, such as ascites and cardiac cachexia, at the time of diagnosis<sup>10</sup>.

Considering the restrictive pathophysiological pattern of the disease, we discuss whether left atrial enlargement should be a marker of functional capacity in the mentioned patients. The objective of this study was to investigate the potential association between left atrial dimension and  $VO_2$  max in patients with endomyocardial fibrosis.

## Methods

The patients selected had been hospitalized for clinical assessment and treatment of endomyocardial fibrosis and had sinus rhythm with biventricular impairment evidenced on ventriculography. This study comprised 38 patients with a mean age of  $37.5 \pm 11.5$  years (range, 11 to 59 years), 25 of the female sex, divided on hospital admission into 2 groups (A and B) according to the NYHA functional class. Group A comprised 12 patients in functional class I or II, and group B comprised 26 patients in functional class III or IV.

All patients, after being stabilized for heart failure, underwent cardiopulmonary exercise testing to assess maximum oxygen consumption ( $VO_2$  max, mL.kg<sup>-1</sup>.min<sup>-1</sup>). The respiratory variables were obtained under standard conditions of temperature, pressure, and humidity (StPD), applying the appropriate correction factors. Both groups underwent maximum exercise testing based on the modified Naughton protocol<sup>11</sup>, using a motorized treadmill (Quinton, model Q65, Seattle, Washington), with variable velocity and tilting.

Commercial echocardiographic equipment was used to assess left atrial dimension (cm). The echocardiographic parameters were determined based on the recommendations of the American Society of Echocardiography<sup>12</sup>.

All patients signed a written consent to participate in the study after being informed about the objectives and methods used. The procedures performed conformed to institutional ethical guidelines, and the institutional review committee approved the protocol with the principles defined by the Helsinki Declaration.

Pearson correlation coefficient and regression analysis were used to investigate the relation between left atrial dimension and  $VO_2\max$  in each group studied. The correlation coefficient was considered statistically significant when  $P < 0.05$ . Tests of parallelism and coincidence between both regression lines were performed for assessing whether the NYHA functional class may influence the potential relation between left atrial dimension and functional capacity. The variables are described in the text as mean  $\pm$  standard deviation.

## Results

The values obtained for  $VO_2\max$  were  $21.8 \pm 4.8$  mL.kg<sup>-1</sup>.min<sup>-1</sup> and  $13.7 \pm 3.5$  mL.kg<sup>-1</sup>.min<sup>-1</sup> in groups A and B, respectively. The left atrial dimension was  $3.7 \pm 0.7$  cm in group A and  $4.4 \pm 0.7$  cm in group B.

Figure 1 shows an inverse correlation between  $VO_2\max$  and left atrial dimension for each group studied separately. The regression line obtained for group B ( $y = 27.4 - 3.1x$ ,  $P = 0.0017$ ) was shifted downwards ( $P = 0.0003$ ) and in parallel ( $P = 0.3727$ ), when compared with the regression line obtained for group A ( $y = 38.8 - 4.6x$ ,  $P = 0.0019$ ), indicating a significant interference of functional class in the correlation found between  $VO_2\max$  and left atrial dimension.

## Discussion

Biventricular endomyocardial fibrosis is clinically characterized by predominantly right heart failure, with descending and prominent elevated jugular venous pressure, quiet precordium, third cardiac sound, and usually huge ascites on physical examination. The patients affected usually have a poor evolution, manifested as a high mortality rate within the first years after diagnosis<sup>13</sup>. Echocardiography performed by experienced professionals is of fundamental importance to confirm the diagnosis in suspicious cases. Normal ventricular cavities or of reduced size with apical obliteration, usually associated with atrioventricular valvular regurgitation and normal or slightly reduced systolic function, are the major characteristics, in addition to an enlarged right or left atrium, or both<sup>14</sup>. The echocardiography may help in the differential diagnosis with other restrictive syndromes, such as amyloidosis and constrictive pericarditis<sup>15</sup>. Fibrous tissue builds up in the endomyocardial region in varied degrees, involving one or both ventricles. Clinical evolution has been related to morphological presentation<sup>7</sup>. In addition, NYHA functional class has been related to survival; therefore, it should be considered in surgical therapeutic decisions<sup>7,16</sup>.

The present study showed that left atrial dimension is related

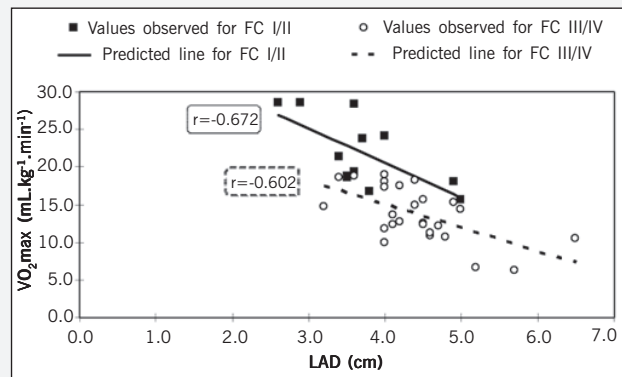


Fig. 1 - Dispersion diagram of left atrial dimension (LAD) versus maximum oxygen consumption ( $VO_2\max$ ) for 2 categories of NYHA functional class.

to  $VO_2\max$  in patients with endomyocardial fibrosis, sinus rhythm, and biventricular impairment. Previous studies<sup>17,18</sup> have reported similar findings in patients with heart failure. As already emphasized, some results have indicated that NYHA functional class interferes with that relation, because the functional class is known to significantly relate to the functional capacity in those patients<sup>8</sup>. The increase in left atrial dimension is a marker of mortality in the general population and also in patients with myocardial infarction<sup>19</sup>. However, the ability for predicting survival based on left atrial dimension should be investigated in patients with endomyocardial fibrosis.

This is the first study indicating an association between a characteristic morphological alteration, represented by left atrial enlargement, and physical capacity impairment in patients with endomyocardial fibrosis. This finding may have prognostic implications, because NYHA functional class has been shown to negatively influence survival. The natural history of patients with endomyocardial fibrosis in functional class I or II is relatively benign as compared with that of patients in functional class III or IV<sup>16</sup>. However, it is yet to be demonstrated whether the characteristic morphological alterations in that disease, such as ventricular dimension and morphology, influence functional capacity. In addition, it is also necessary to investigate whether our findings can be applied to patients who are not in sinus rhythm and have isolated right or left ventricular impairment.

In patients with dilated cardiomyopathy, left atrial volume has been associated with ventricular remodeling, diastolic dysfunction, and the degree of mitral regurgitation<sup>20</sup>. In endomyocardial fibrosis, the enlargement in left atrial dimension may be related to the presence of mitral regurgitation, diastolic dysfunction, or degree of fibrous tissue build-up. The cause of such enlargement should be better investigated.

Previous studies have reported that, in patients without any antecedent of atrial arrhythmias or valvular heart disease, left atrial volume reflects the degree of diastolic dysfunction<sup>21</sup>. Diastolic dysfunction is recognized as an important prognostic factor in several heart diseases, and endomyocardial fibrosis is a disease model characterized by that dysfunction<sup>22</sup>. However, the indices obtained on Doppler are influenced by multiple factors. In contrast, left atrial dimension is less influenced by acute alterations and reflects the duration and severity of the diastolic dysfunction<sup>23-24</sup>.

In patients with endomyocardial fibrosis, the reduction in com-



pliance caused by fibrous tissue build-up leads to an increase in left atrial pressure to maintain adequate left ventricular filling<sup>25</sup>. Therefore, the increase in left atrial pressure causes atrial dilation. From the pathophysiological viewpoint, our findings may indicate that the left atrial dimension corresponds to the degree of restriction in ventricular filling, and, therefore, should be an accurate marker of the stage of the disease and reflect the degree of diastolic function impairment. In addition, left atrial dimension has proved to be an important predictor of atrial fibrillation. Previous studies have reported

that atrial fibrillation is present in 36.2% of the patients with endomyocardial fibrosis and biventricular or predominantly right ventricular impairment<sup>26</sup>. In addition, in these patients, atrial fibrillation is associated with a worse prognosis, but the study showed that surgery potentially reversed that poor evolution.

Our findings allow the use of a morphological parameter, such as left atrial dimension, which is easily obtained on echocardiography, for estimating a more complex and difficult to assess index, such as  $VO_2$ max.

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