Original Article

Left Ventricular Mass in Patients with Heart Failure

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Objective

To assess left ventricular mass in patients with heart failure and its correlations with other clinical variables and prognosis.

Methods

The study comprised 587 patients aged from 13.8 years to 68.9 years, 461 (78.5%) being males and 126 (21.5%) females. Left ventricular mass was estimated by using M-mode echocardiography and was indexed by height.

Results

The left ventricular mass index ranged from 35.3 g/m to 333.5 g/m and increased with age. The left ventricular mass index was greater in males (mean, 175.7 g/m) than in females (mean, 165.7 g/m). The left ventricular mass index was greater in patients with hypertensive cardiomyopathy (mean of 188.1 g/m), with idiopathic dilated cardiomyopathy (mean, 177.7 g/m) and with cardiomyopathies of other etiologies (mean, 175.1 g/m) than in patients with chagasic (mean, 164.3 g/m) or ischemic (mean, 162 g/m) cardiomyopathy. The left ventricular mass index in patients with heart failure showed a correlation with age, sex, etiology, and left atrial diameter. The correlation with left ventricular ejection fraction was negative: the increase in the left ventricular mass index was associated with a reduction in ejection fraction. The relative risk of death was 1.22 for each 50-g/m increase in the left ventricular mass index.

Conclusions

The estimate of left ventricular mass may contribute to the prognostic assessment of patients with heart failure.

Key words

left ventricular mass, left ventricular hypertrophy, heart failure, prognosis

Left ventricular hypertrophy was identified as a risk factor of cardiovascular morbidity and mortality in the Framingham Study [1-3].

Patients with heart failure due to ventricular dysfunction undergo cardiac anatomical changes, which are included under the concept of cardiac remodeling [4]. Remodeling occurs in different clinical circumstances and in different patients in heterogeneous ways.

From the clinical point of view, great differences are observed in the left ventricular mass estimated on physical examination, on electrocardiography, or by use of the dimension of the cardiac image on chest radiography. Among patients with heart failure of the same etiology, some with a similar functional condition were observed to have different magnitudes of the cardiac image on chest radiography.

From the echocardiographic point of view, greater mortality and hospitalization rates due to cardiovascular diseases were observed in patients with left ventricular dysfunction and left ventricular hypertrophy. The echocardiographic estimate of left ventricular mass added prognostic information to other cardiovascular risk factors. However, assessment of left ventricular hypertrophy, as compared with other clinical variables, suggested independence between left ventricular hypertrophy and left ventricular ejection fraction [5], a different finding from that of our initial study. The correlation tests of left ventricular mass with age, duration of symptoms, left ventricular end-diastolic pressure, and pulmonary artery systolic and occlusion pressures did not show statistically significant values. However, the correlation with the left ventricular ejection fraction calculated on echocardiography was significant. The stepwise regression analysis showed a negative correlation between left ventricular mass and left ventricular ejection fraction [6].

On autopsy study, patients with hypertensive, ischemic, and idiopathic cardiomyopathies had similar weights, which were greater than those of patients with cardiomyopathy due to Chagas' disease [7].

Therefore, the clinical observation, echocardiographic data, and autopsy studies allow the hypothesis that the left ventricular mass may be a relevant variable for the prognosis of patients with heart failure. In this context, we formulated the hypothesis that left ventricular mass may also provide prognostic information about patients with symptomatic heart failure.

This study aimed at assessing, in a large case series of patients with heart failure being followed up for more than 10 years, the distribution of left ventricular mass on echocardiography, its correlations with other clinical variables, and its potential prognostic influence.

Methods

A cross-sectional study [8] was carried out for assessing left ventricular mass in a cohort of patients with heart failure being followed up on an outpatient basis.

The diagnosis of heart failure was established based on the Framingham criteria [9], and the diagnosis of the etiology of heart failure was based on previously established criteria [10] and on the International Classification of Diseases 1993, 10th review (ICD 10).

Patients aged < 75 years diagnosed with symptomatic heart failure due to systolic ventricular dysfunction were included in the study.

Patients with the following characteristics were excluded from the study: heart failure due to cardiomyopathies indicated for surgical treatment (myocardial revascularization, aneurysmectomy, valvuloplasty, or valvular replacement); hypertrophic cardiomyopathy; chronic obstructive pulmonary disease; recent acute myocardial infarction; and unstable angina. Patients with the following characteristics were also excluded from the study: creatinine clearance lower than 30 mL/kg/min; liver failure; peripheral arterial disease; cerebrovascular disease; type I diabetes mellitus; recent infection; neoplasias; or active peptic ulcer disease.

This study comprised 587 patients with heart failure, who were followed up from April 1991 to December 2000. Their ages ranged from 13.8 to 68.9 years (mean of 45.6 years, standard deviation of 10.3 years), 461 (78.5%) were males and 126 (21.5%) were females.

The time elapsed between symptom onset and entrance into the study ranged from 6.9 days to 243.5 months (mean, 50.1 months; standard deviation, 49 months).

Heart failure was attributed to ischemic cardiomyopathy in 114 (19.4%) patients, chagasic cardiomyopathy in 97 (16.5%), hypertensive cardiomyopathy in 82 (14%), and other etiologies in 73 (12.4%). In 221 (37.7%) patients, heart failure was attributed to idiopathic dilated cardiomyopathy.

Echocardiographic, radioisotopic, electrocardiographic, and functional characteristics of the population studied are shown in table 1.

The patients were followed up on an outpatient care basis. The clinical treatment included dietary guidance, instruction about the general principles of treatment, and prescription of medications adjusted to their needs and tolerance. The medications included angiotensin-converting-enzyme inhibitors, diuretics, and digitalis. Beta-blockers were gradually introduced in the treatment from 1997 onwards.

Data on evolution were supplemented by a review of hospital records, telephone contact by the researchers, and research in the ProAim (Programa de Aprimoramento de Informações de Mortalidade do Município da Cidade de São Paulo – Program on improvement of the information on mortality in the city of São Paulo).

Echocardiographic measurements were taken according to the criteria recommended by the American Society of Echocardiography[11].

Left ventricular mass was estimated by use of the following formula [12]: LVM (grams) = 0.8 X {1.04 X [(LVID + IST + PWT)^3– (LVID)^3]} + 0.6, where: LVM = left ventricular mass; PWT = left ventricular posterior wall thickness; IST = interventricular septum thickness; LVID = left ventricular inner diameter.

The left ventricular mass was indexed by the patient's height (g/m) [12], and the term "ventricular mass index" began to be used. For comparisons with the left ventricular mass index, this indexation was also performed for other echocardiographic variables.

The left ventricular mass index was studied in regard to age, sex, duration of symptoms, left and right ventricular ejection fraction

Table I - Laboratory characteristics of the population studied		
Variables	N	Mean (standard deviation)
Echocardiographic data		
Left ventricular posterior wall thickness (mm)	587	8.3 (1)
Interventricular septum thickness (mm)	587	8.3 (1.1)
Left ventricular diastolic diameter (mm)	587	74.2 (9.5)
Left atrial diameter (mm)	584	46.9 (8.2)
Left ventricular ejection fraction (%)	587	36.2 (7.8)
Relative wall thickness *	587	0.23 (0.05)
Radioisotopic ventriculography		
Left ventricular ejection fraction (%)	481	22.3 (8)
Right ventricular ejection fraction (%)	325	24 (8.2)
Dynamic electrocardiography		
Maximum heart rate (bpm)	238	129 (26)
Minimum heart rate (bpm)	238	55.2 (13.6)
Nonsustained ventricular tachycardia (n)	149	92.8 (439.1)
Cardiopulmonary exercise test		
Maximum O$_2$ consumption (mL/kg/min)	102	15.1 (5.3)

* sum of the measures of posterior wall thickness and interventricular septum thickness divided by the left ventricular diastolic diameter.

on radioisotopic ventriculography, maximum O$_2$ consumption on cardiopulmonary exercise testing, maximum and minimum heart rates, and the presence of nonsustained ventricular tachycardia on 24-hour dynamic electrocardiography.

The demographic and functional variables of the population studied and the left ventricular mass index were initially examined by using exploratory descriptive analysis, with identification of the minimum, maximum, and mean values, median, and standard deviation of the variables studied. Then the left ventricular mass index was studied in regard to the probability of survival by using the Kaplan Meier method [13]. Death was considered an event; the surgical interventions, including transplantation, were considered censored data. The comparisons were performed by means of the log-rank and Breslow tests [13].

To assess the relations of the left ventricular mass index with the demographic and functional variables, multivariate linear regression was used.

The relative risk of death was estimated by using the Cox proportional hazards regression model [14]. An analysis of residues was performed to assess whether the suppositions performed when using the Cox model were satisfied. The results are shown as relative risk, P value, and respective 95% confidence intervals.

The statistical significance level adopted was P < 0.05. The calculations were performed by using SPSS software, version 10.0, and SAS software, version 8.2.

The protocol was approved by the Institutional Committee of Research in Human Beings.

Results

The left ventricular mass index ranged from 35.3 g/m to 333.5 g/m (mean, 173.5 g/m; standard deviation, 44 g/m) and increased

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according to age categorized in quartiles (fig. 1). The left ventricular mass index ranges according to the age groups were as follows: from 79.7 g/m to 332.6 g/m (mean, 168.5 g/m; standard deviation, 41.4 g/m) in patients aged < 39.3 years; from 96.2 g/m to 333.5 g/m (mean, 173.2 g/m; standard deviation, 46.8 g/m) in patients aged from 39.3 years to 46.4 years; from 86.5 g/m to 325.5 g/m (mean, 175.3 g/m; standard deviation, 44.4 g/m) in patients aged from 46.4 to 52.9 years; and from 35.3 g/m to 309.3 g/m (mean, 176.1 g/m; standard deviation, 42.6 g/m) in patients aged > 52.9 years.

The left ventricular mass index was greater among males [range, 35.3 g/m to 333.5 g/m (mean, 175.7 g/m; standard deviation, 44.3 g/m)] than among females [range, 88.2 g/m to 332.6 g/m (mean, 165.7 g/m; standard deviation, 42.3 g/m)] (fig. 2).

Left ventricular mass index was lower in patients with chagasic and ischemic cardiomyopathies than in those with hypertensive cardiomyopathy, idiopathic dilated cardiomyopathy, and cardiomyopathies of other etiologies (fig. 3). The left ventricular mass index ranges according to the etiologies of cardiomyopathy were as follows: from 96.2 g/m to 309.3 g/m (mean, 188.1 g/m; standard deviation, 44.6 g/m) in patients with hypertensive cardiomyopathy; from 35.3 g/m to 332.6 g/m (mean, 177.7 g/m; standard deviation, 45.9 g/m) in patients with idiopathic dilated cardio-

myopathy; from 88.2 g/m to 333.5 g/m (mean, 175.1 g/m; standard deviation, 50.3 g/m) in patients with cardiomyopathy of other etiologies; from 97.5 g/m to 239.6 g/m (mean, 164.3 g/m; standard deviation, 33.7 g/m) in patients with chagasic cardiomyopathy; and from 86.5 g/m to 264.2 g/m (mean, 162 g/m; standard deviation, 39.5 g/m) in patients with ischemic cardiomyopathy.

The left ventricular mass index categorized into quartiles showed no significant difference in regard to the probability of survival (fig. 4).

The left ventricular mass index increased 0.39 g/m for each increase in year of the patient's age, and the other variables (sex, etiology, left ventricular ejection fraction on radioisotopic ventriculography, left atrial diameter) remained constant (tab. II). The left ventricular mass index in male patients was 11.2 g/m greater than that in female patients.

The left ventricular mass index in patients with hypertensive cardiomyopathy, compared with that in patients with ischemic car-
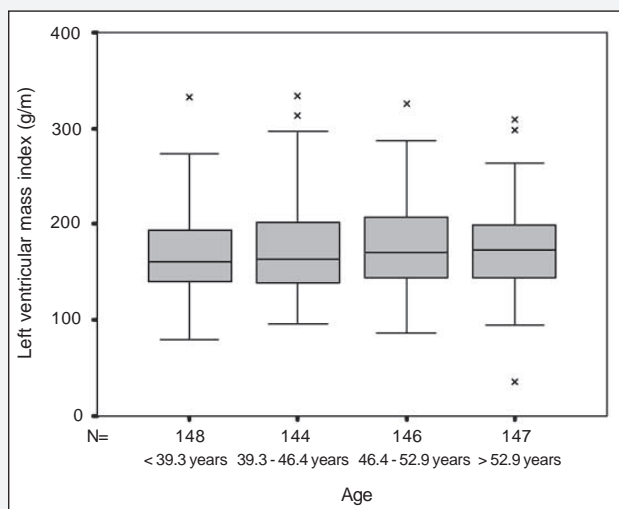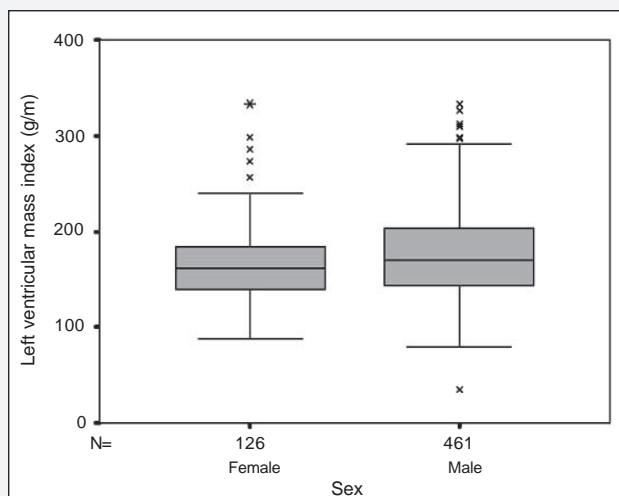

Fig. 3 - Left ventricular mass index in regard to etiology.

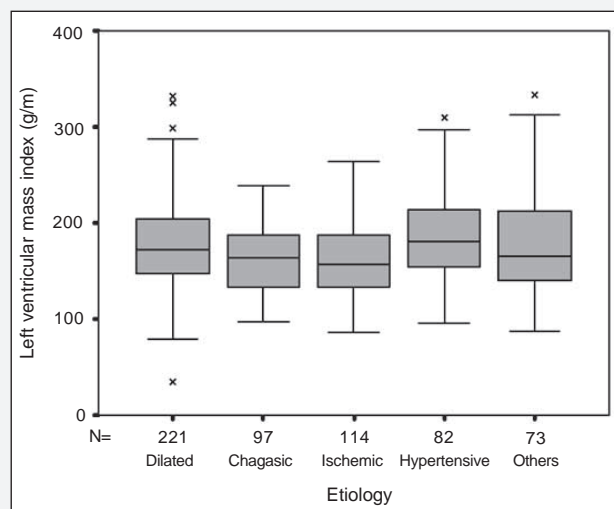
Fig. 1 - Left ventricular mass index in regard to age.

Quartiles of the left ventricular mass index:

—— Less than 140.8 g/m

----- From 140.8 g/m to 166.6 g/m

Test	P-value
Log-Rank	0.2060
Breslow	0.1458

········ From 166.6 g/m to 201.1 g/m

—— More than 201.1 g/m

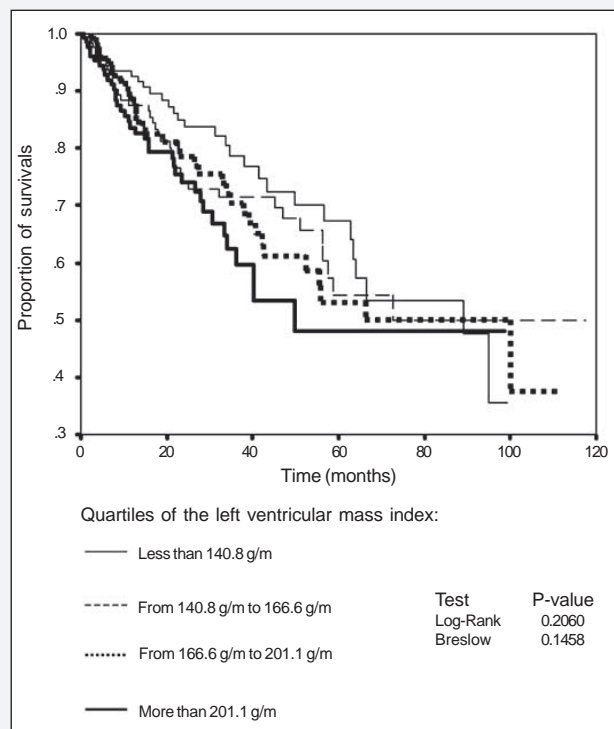Fig. 4 - Left ventricular mass index in regard to the chance of survival.

Fig. 2 - Left ventricular mass index in regard to sex.

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diomyopathy, was 27.4 g/m greater. The left ventricular mass indices of patients with cardiomyopathy of unknown etiology and with cardiomyopathy of other etiologies were 16.7 g/m and 12.9 g/m greater, respectively, and that of patients with chagasic cardiomyopathy showed no statistically significant difference when compared with that in patients with ischemic cardiomyopathy.

The left ventricular mass index increased 6.96 g/m for each 5-mm/m increase in the left atrial diameter.

The left ventricular mass index on radioisotopic ventriculography had a negative relation with left ventricular ejection fraction. The left ventricular mass index decreased 1.2 g/m for each 1-unit increase in ejection fraction.

For each 1-g/m increase in the left ventricular mass index, the relative risk of death increased 0.4% (P = 0.0418) (95% CI: 0 to 1%). Because the left ventricular mass index in our case series ranged from 35.35 to 333.52 g/m, the relative risk of death was 1.22 (95% CI: 1 to 1.49) for each 50-g/m increase.

Discussion

This study comprised a large cohort of patients with symptomatic heart failure of different etiologies, including Chagas' heart disease, who were followed up on an outpatient care basis at a single institution for 10 years. Patients with cardiomyopathy of unknown etiology (idiopathic, 37.7%) were the most frequent, followed by patients with ischemic cardiomyopathy (19.4%), chagasic cardiomyopathy (16.5%), and hypertensive cardiomyopathy (14%). This etiologic distribution differs from that of other case series, in which ischemic cardiomyopathy (34% to 60% of the cases)[15-17], idiopathic cardiomyopathy (18.2% to 59% of the cases)[16,17], and hypertensive cardiomyopathy (3.8% to 23.6% of cases)[16] predominated. Therefore, our results were assessed according to these characteristics, including the etiologic distribution.

M-mode echocardiography was used to assess left ventricular mass. Alterations in ventricular dimension and geometry may induce inaccuracies in the estimate of left ventricular mass index. The left ventricular mass was indexed by height because patients with heart failure may vary in weight due to fluid retention or loss. This indexation was validated in the literature in a study with extreme methodological strictness, which assessed 864 individuals and found an association between left ventricular mass and height (r=0.39, P < 0.001 in males; r=0.23, P < 0.001 in females)[12]. In addition, height is strongly associated with lean body mass, which is an excellent predictor of left ventricular mass[18]. Despite of restrictions,

M-mode echocardiography has been used in large population studies, including those showing the important relation between left ventricular mass and cardiovascular morbidity and mortality[12,19].

Age influenced left ventricular mass index in an independent way. The 1-year increase in age was associated with a 0.39-g/m increase in left ventricular mass index. This observation differs from the previous population studies of individuals with no cardiomyopathy, in which age had no influence on left ventricular mass[20,21]. On the other hand, the Framingham study showed a relation between age and left ventricular mass in patients with cardiomyopathy, but this relation was not shown in patients without cardiomyopathy[22]. Therefore, the appearance of heart failure may represent a modulatory factor of the relations between left ventricular mass and age.

Sex influenced the left ventricular mass index adjusted for height in an independent way; the left ventricular mass index was 11.2 g/m greater in males as compared with that in females. This finding confirms data of previous epidemiologic studies including hypertensive patients[12,21,23,24]. Therefore, in regard to sex and with adjustment of the other variables of comparison, patients with heart failure maintain the difference in left ventricular mass.

The left ventricular mass index was higher in patients with hypertensive cardiomyopathy, followed by those with idiopathic dilated cardiomyopathy. The left ventricular mass index in patients with ischemic cardiomyopathy and chagasic cardiomyopathy did not show a statistically significant difference. A study of patients with aortic stenosis showed that the increase in left ventricular mass resulted from a combination of hypertrophy and hyperplasia of myocytes[25]. Therefore, the mechanisms acting on the increase in ventricular mass may act differently according to the etiology of the cardiomyopathy that causes heart failure.

The relation between the left atrial diameter on echocardiography and the left ventricular mass index was assessed. The left ventricular mass index increased 6.96 g for each 5-mm increase in the left atrial diameter. In this study, the numerical estimate of this relation is noteworthy. One hypothesis is that the same variables that influence ventricular mass may also influence left atrial diameter[26,27]. On the other hand, the increase in left ventricular mass could contribute to an increase in the atrial dimensions, due to both hemodynamic and biochemical factors. Although the hypothesis of the left atrial enlargement secondary to left ventricular diastolic dysfunction may be attractive, a study in patients with arterial hypertension by use of Doppler diastolic indices did not show this occurrence[28]. On the other hand, this same study showed that the left atrial size in hypertensive patients with left ventricular hypertrophy on electrocardiography did not depend on left ventricular mass[28]. Therefore, a relation between left atrial diameter and left ventricular mass in patients with heart failure exists, but not in myocardial hypertrophy of patients with arterial hypertension.

The left ventricular ejection fraction on radioisotopic ventriculography showed a negative relation with the left ventricular mass index. A 1-unit increase in ejection fraction was associated with a 1.2-g/m decrease in the left ventricular mass index. The association of left ventricular mass index and left ventricular ejection fraction on radioisotopic ventriculography may contribute to explain the lower survival resulting from an increase in left ventricular mass index. The influence of the decrease in ejection fraction leading to an increase in mortality was observed in other studies[15,29].

Table II - Relations of the left ventricular mass index with the demographic and functional variables			
Varible	Estimate	Standard error	P value
Age	0.3925	0.1696	0.0210
Sex (male)	11.2047	4.2188	0.0081
Hypertensive etiology	27.3629	5.8058	0.0261
Idiopathic etiology	16.6845	4.0165	<0.0001
Other etiologies	12.9527	5.3999	<0.0001
Left atrial inner diameter	13.9206	3.5392	<0.0001
Left ventricular ejection fraction	-1.2411	0.2194	<0.0001
Ejection fraction obtained on radioisotopic ventriculography.			

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Although the comparison of the probabilities of survival of patients, whose left ventricular mass indices were categorized in quartiles, showed no statistically significant difference, the Cox proportional hazards regression model revealed that for each 1-g/m increase in left ventricular mass index, the relative risk of death increased 0.4%. Because the left ventricular mass index in our case series ranged from 35.35 g/m to 333.52 g/m, the relative risk of death was 1.22 for each 50-g/m increase in the left ventricular mass index. In the Framingham study with patients without cardiomyopathy, for each 50-g/m increase in the left ventricular mass, a relative risk of death due to heart diseases of 1.73 was observed in males and of 2.12 in females [30]. In a case series of elderly patients without cardiomyopathy, whose ages ranged from 59 years to 90 years, the incidence of coronary events for each 50-g/m increase in left ventricular mass was 1.67 in males and 1.60 in females [31]. Therefore, the increase in left ventricular mass index is an unfavorable prognostic factor.

It is worth noting that the case series studied comprises symptomatic patients in an advanced phase of the disease. These observations, however, may not be applicable to the general population or patients with heart failure in another phase of clinical evolution.

In conclusion, the influence of left ventricular mass was not very strong, but could contribute to the prognostic assessment of patients with heart failure. Therefore, the relations with other variables, including the negative correlation with left ventricular ejection fraction on radioisotopic ventriculography, require further studies.

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