

Correlation between Diastolic Function and Maximal Exercise Capacity on Exercise Test

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Abstract

Background: Increased pulmonary capillary pressure (PCP) is one of the mechanisms of exercise intolerance. Assessment of the diastolic function by echocardiography (ECHO) enables estimation of PCP.

Objective: To identify variables that determine the exercise capacity in patients undergoing routine exercise test (ET), conventional ECHO, and tissue Doppler imaging (TD).

Methods: A total of 640 patients undergoing ET, ECHO, and TD were retrospectively studied. Patients with ejection fraction < 55% were excluded. Mitral annulus velocities by conventional Doppler imaging were obtained in early diastole (E) and late diastole (A), and TD of the mitral annulus measured early diastole (e') and late diastole (a') velocities. $E/e' > 10$ was considered an estimate of increased PCP. Maximal exercise capacity was analyzed by the number of metabolic equivalents (MET). The patients were divided into two groups for analysis: MET < 7 (n=48) and MET > 7 (n=572). Morise score showed a population at low risk (60%) for coronary artery disease (CAD).

Results: The number of patients with $E/e' > 10$ was significantly higher in the MET < 7 group in relation to the MET > 7 group (41.7% vs 9.4%, $p=0.001$), and so was the presence of any degree of diastolic dysfunction (76.6% vs 34.1% $p=0.001$). Using logistic regression analysis, age, female gender and A velocity (late diastole) were the independent variables related to a low exercise capacity (MET < 7).

Conclusion: Diastolic dysfunction as determined by ECHO, female gender, and age are associated with a lower exercise capacity in a population at low risk for CAD. (Arq Bras Cardiol 2011; 96(2): 107-113)

Keywords: Ventricular dysfunction; exercise test; exercise; diastole; echocardiography, tissue Doppler.

Introduction

Exercise capacity is influenced by innumerable factors, such as advanced age¹, comorbidities (metabolic syndrome and hypertension)², obesity³ and previous cardiorespiratory fitness¹. Identification of other factors that modify the exercise capacity is highly relevant, because its reversal can improve the quality of life of the patients and have an effect on survival, since exercise capacity is associated with prognosis both in healthy individuals⁴⁻⁶ and in patients with heart diseases⁷.

In an attempt to explain the cardiac mechanisms that decrease exercise capacity, ejection fraction did not show a significant correlation, perhaps for being dependent on the preload⁸. However, maximal exercise capacity, as well as the symptoms triggered by exercise, are directly related to increased pulmonary capillary pressure and, therefore, to increased left ventricular filling pressures. Filling pressures, in turn, are directly related to the left ventricular diastolic function^{9,10}.

Recent clinical studies observed a significant correlation between exercise capacity and diastolic function parameters, especially in patients with cardiovascular disease¹¹.

Recent advances in tissue Doppler imaging improved the accuracy of echocardiography in the identification of abnormalities of left ventricular early-diastole¹², including the estimation of filling pressures¹³. Consequently, the use of tissue Doppler imaging and of the analysis of diastolic function may be useful to explain the correlation between the presence of diastolic dysfunction and maximal exercise capacity on exercise test.

The objective of the present study was to analyze the exercise capacity and its correlation with diastolic function, as well as with the different clinical parameters in a population predominantly consisting of individuals at a low risk for coronary artery disease.

Methods

This is a retrospective cross-sectional study conducted from July 2007 to January 2008, which evaluated 640 individuals with a mean age of 49 ± 13 years. The study was approved by the Research Ethics Committee of *Instituto de Cardiologia do Distrito Federal*.

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Manuscript received October 08, 2009; revised manuscript received

November 16, 2009; accepted March 11, 2010.

All individuals underwent exercise test and transthoracic echocardiography within an interval of up to 30 days¹⁴. Patients with ejection fraction < 55% were not included in the analysis.

Functional capacity was assessed by the peak metabolic equivalent (MET peak), indirectly obtained by formulas¹⁵, according to the maximum slope and speed achieved in an incremental exercise treadmill test, with the ramp protocol adjusted to the individual.

Echocardiographic study was performed with two-dimensional images of the M mode and with pulsed Doppler using an echocardiographic equipment (Philips HDI 5000) with a 2 to 4 MHz multifrequency transducer. Mitral inflow velocities were recorded using pulsed Doppler in the apical 4-chamber view, with a sample volume of 5 mm at the tip of the mitral leaflets. Early diastolic velocity (E), late diastolic velocity (A) and deceleration time were measured; the E/A ratio was also calculated¹⁶. Using the apical 4-chamber view, a 2-mm sample volume was placed in the junction of the LV wall with the septal mitral annulus in order to record tissue Doppler, deriving the tracing velocities during systole (S), early diastole (e'), and late diastole (a')¹². The E/e' ratio was calculated to estimate LV filling pressures, and values greater than ten (10) were considered increased filling pressures¹². The cut-off point for the E/e' ratio was set at 10 based on data from Burgess et al's study, in which E/e' > 10 ratios (with e' of the septal annulus) were the optimal index for the identification of patients whose filling pressures increase with exercise, with sensitivity of 71% and specificity of 69%¹⁷.

The diastolic function was analyzed according to the protocol used in our laboratory, starting with the assessment of the E and A velocities of the mitral pulsed Doppler, and E/A ratio calculation. Next, the tissue Doppler velocities of the septal annulus (e' and a') are obtained, and the E/e' ratio is calculated. Using the two-dimensional image, the left atrial (LA) volume is evaluated. When in doubt about the degree of diastolic dysfunction using the methods previously described, the pulmonary vein flow velocities or Valsalva maneuver are performed. Based on these parameters, the diastolic function is classified as: normal (E/A>0.8, e'>8 cm/s, normal LA volume; E/e' ratio was not considered); diastolic dysfunction with abnormal relaxation pattern (E/A<0.8, e'<8 cm/s, variable LA volume, and variable E/e'); pseudonormal diastolic dysfunction (E/A>0.8, e'<8 cm/s, LA volume usually increased, and E/e'>15); and restrictive diastolic dysfunction (E/A> 1.8, e'<8 cm/s, LA volume usually increased, and E/e'>15). This methodology is based on several classifications of analysis of the diastolic function^{12,18,19} and is relatively easy to use in the daily practice of echocardiography laboratories.

For the statistical analysis, the individuals were divided into two groups: MET<7 (n=48) and MET≥7 (n=572), according to their exercise capacity.

Individuals with MET peak < 7 show low physical capacity, usually associated with functional limitations and symptoms, in addition to being exposed to a higher risk of cardiovascular events^{4-6,15}.

The chi square test and Fisher test were used to analyze the association between the groups and the classificatory variables. The Wilcoxon test was used for comparison of the means between the two groups. The variables showing statistical significance in the univariate analysis were used in the adjustment

of the logistic regression model. P values < 0.05 were considered statistically significant. The Stata 8.0 and SAS software programs were used for processing and statistical analysis.

Results

The baseline clinical characteristics and main echocardiographic measurements are described in Tables 1 and 2, respectively.

Analysis of the diastolic function

Normal diastolic function was observed in 62% of the individuals; 30.4% showed diastolic dysfunction with relaxation abnormality; 6.1% showed pseudonormal diastolic dysfunction; 0.32%, restrictive diastolic dysfunction; and 1.1%, undetermined degree of diastolic dysfunction. Only 12.7% had increased filling pressures (as assumed by an E/e' ratio >10). Of these 12.7%, 17 patients (2.6%) had normal diastolic function and normal exercise capacity (MET > 7).

Risk of CAD in the population

The probability of CAD was calculated based on the Morise score²⁰. We found 60% of individuals with low probability, 39% with moderate, and 1% with high probability of CAD. Therefore, most of the patients had low probability of CAD.

Table 1 - Baseline clinical characteristics

Parameters	Individuals studied (n=640)
Male gender	60%
Diabetes mellitus	7.8%
Hypertension	37.6%
Cigarette smoking	11.5%
Dyslipidemia	33.4%
Obesity	26.8%
Positive exercise test	11.8%

Table 2 - Baseline echocardiographic characteristics

Parameters	Values (mean ± SD)
LV mass index (g/m ²)	89.8 ± 25.3
LV diastolic diameter (mm)	48.3 ± 4.7
LV systolic diameter (mm)	30.2 ± 4.7
Mitral E wave velocity (cm/s)	72.2 ± 17.1
Mitral A wave velocity (cm/s)	62.7 ± 18.3
E/A ratio	1.24 ± 0.47
E wave deceleration time (ms)	212.7 ± 57.6
Mitral annulus e' velocity (cm/s)	9.9 ± 3.9
Mitral annulus a' velocity (cm/s)	9.9 ± 3.8
Mitral annulus S velocity (cm/s)	8.9 ± 2.8
E/e' ratio	7.8 ± 2.9
Ejection fraction (%)	66.8 ± 7.3

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Determinants of functional exercise capacity on exercise test

Univariate analysis of the exercise capacity in MET was carried out in relation to clinical and echocardiographic parameters. We observed that the clinical parameters that correlated with a low functional capacity (MET < 7) were female gender, age, presence of diabetes mellitus (DM), presence of hypertension, and obesity (Table 3). In relation to the echocardiographic parameters, we observed that the LV mass index, A wave velocity of the mitral flow velocity, E/A ratio of the mitral flow, e' wave velocity of tissue Doppler of the mitral annulus, S wave velocity of tissue Doppler of the mitral annulus, and the E/e' ratio were associated with MET < 7 (Table 4).

The clinical and echocardiographic parameters which were independently associated with a low exercise capacity in the adjusted logistic regression model were age, female gender, and A wave velocity of the mitral flow (Table 5).

The comparative analysis of the MET < 7 and MET > 7 groups in relation to the presence of increased filling pressures (Graph 1) showed that 41.6% of the individuals with low functional capacity had a E/e' ratio > 10, whereas only 9.4% of the individuals had a good functional capacity. The same was observed in relation to the presence of diastolic dysfunction: 76.6% of the patients with low functional capacity had some degree of diastolic dysfunction in comparison to 34.1% of the patients with a better functional capacity (Graph 2).

Discussion

The novel and important finding of the present study is that even in patients at low risk of CAD there is a significant correlation between diastolic function and exercise

capacity. Another significant finding corroborating other studies^{1,10,21} is that clinical parameters such as advanced age and female gender are independent predictors of a low functional capacity.

Undoubtedly, the presence of diastolic dysfunction has a physiological ground on the decreased exercise capacity since, during exercise, the maximal cardiac output is dependent

Table 4 - Echocardiographic parameters in the univariate analysis

Echocardiographic parameters	MET < 7 (n=48)	MET ≥ 7 (n=572)	p
LV mass index (g/m ²)	101 ± 34	88 ± 25	0.011
LV diastolic diameter (mm)	49 ± 6	48 ± 4	0.384
LV systolic diameter (mm)	32 ± 7	30 ± 4	0.081
Mitral E wave velocity (cm/s)	73 ± 16	72 ± 17	0.757
Mitral A wave velocity (cm/s)	82 ± 25	61 ± 17	<0.001
E/A ratio	0.96 ± 0.4	1.27 ± 0.5	<0.001
Deceleration time	217 ± 43	212 ± 59	0.330
Mitral annulus e' velocity (cm/s)	7.4 ± 2	10.2 ± 3	<0.001
Mitral annulus a' velocity (cm/s)	10.2 ± 3	9.8 ± 2	0.560
Mitral annulus S velocity (cm/s)	8.0 ± 2	9 ± 2	<0.001
E/e' ratio	10.7 ± 4.1	7.5 ± 2.7	<0.001

Table 3 - Clinical parameters in the univariate analysis

Clinical parameters		MET < 7 (n=48)	MET ≥ 7 (n=572)	p
Age (years)		62.1 ± 10.6	48.3 ± 12.4	0.001
Gender	Female	15.2% (39)	84.8% (217)	0.001
	Male	2.3% (9)	97.7% (375)	
Diabetes mellitus	No	6.1% (36)	93.9% (554)	0.001
	Yes	24% (12)	76% (38)	
Hypertension	No	4.0% (16)	96% (383)	0.001
	Yes	13.3% (32)	86.7% (209)	
Cigarette smoking	No	7.6% (43)	92.4% (523)	0.796
	Yes	6.8% (5)	93.2% (69)	
Dyslipidemia	No	5.3% (24)	94.7% (450)	0.001
	Yes	12.6% (24)	87.3% (190)	
CAD*	No	6.8% (31)	93.2% (453)	0.326
	Yes	9.1% (17)	90.9% (187)	
Obesity	No	5.5% (27)	94.5% (489)	0.001
	Yes	13.9% (21)	86.1% (151)	
Positive ET†	No	7.4% (42)	92.6% (570)	0.718
	Yes	8.6% (06)	91.4% (70)	

*CAD - coronary artery disease; †ET - exercise test.

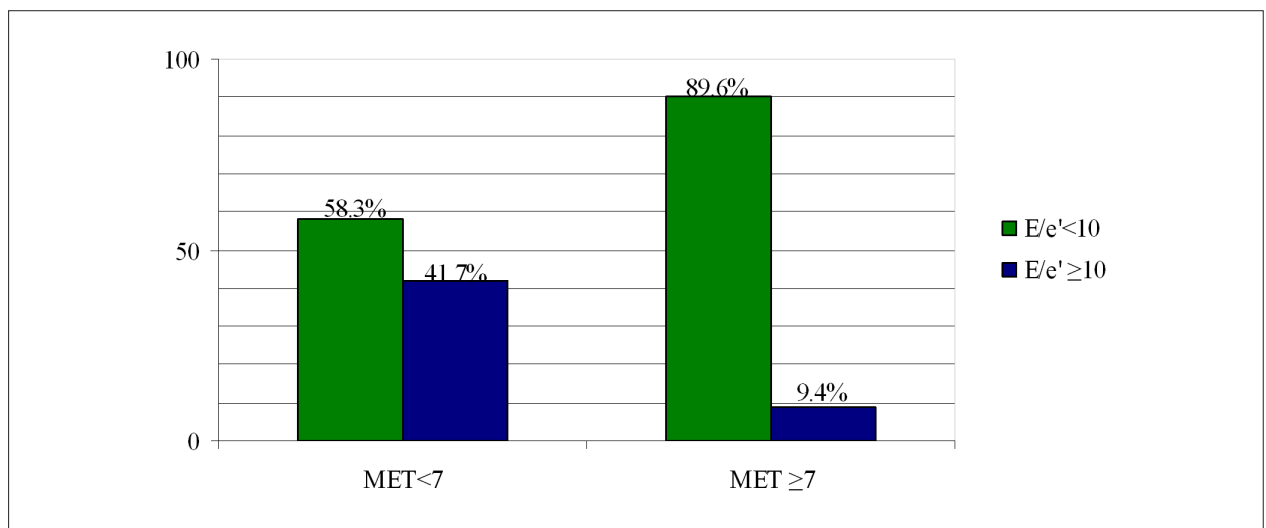
on the diastolic filling. In exercise-induced tachycardia, the diastole is shortened. If diastole is accompanied by left ventricular relaxation and filling abnormalities, the lowest

filling rates are achieved and become inadequate to supply the cardiac output required during exercise, with a subsequent increase in filling pressures and decrease in the maximal capacity²². The more abnormal the baseline diastolic function, the lower the exercise capacity.

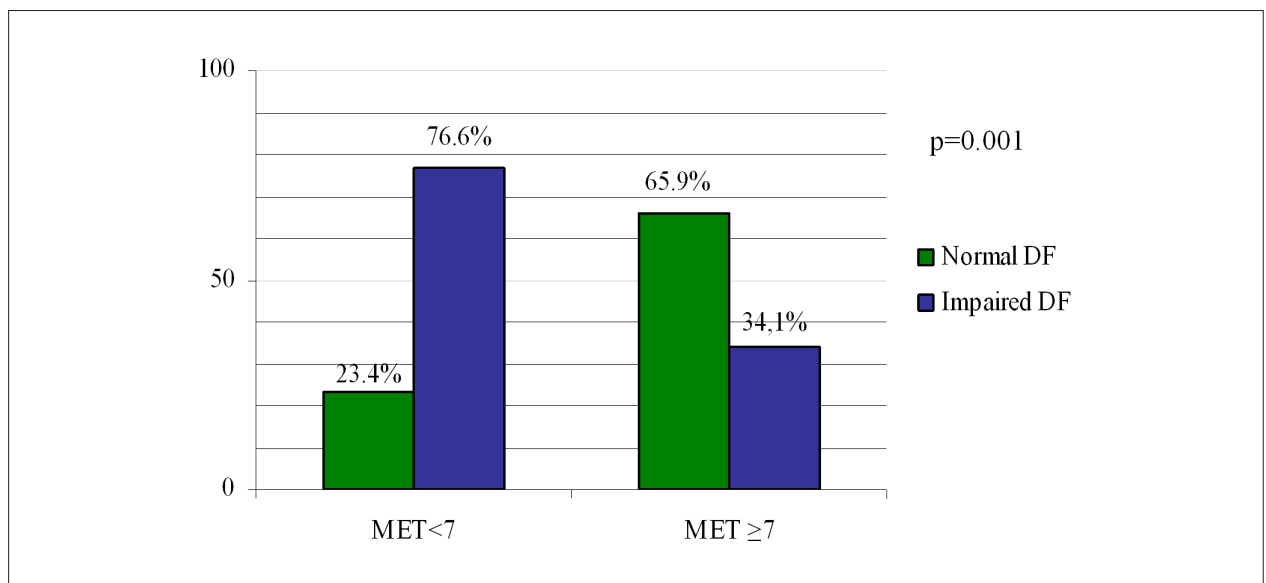
Table 5 - Clinical and echocardiographic determinants of low exercise capacity (logistic regression)

Independent parameters	MET < 7 (n=48)	MET ≥ 7 (n=592)	OR	P
Age (years)	62±11	48 ± 2	1.09	<0.001
Female gender	39 (15.2%)	217 (84.8%)	11.37	<0.001
Mitral A wave velocity (cm/s)	82 ± 25	61 ± 17	1.03	0.004

Several studies have demonstrated a good correlation between tissue Doppler of the mitral annulus and functional exercise capacity^{23,24}, probably due to the association of the E/e' ratio with left ventricular filling pressures^{19,25}. However, most of these studies were conducted in populations at high cardiovascular risk or in patients with proven cardiovascular disease. Recently, Grewal et al¹⁰ observed a good correlation between the E/e' ratio and exercise capacity in a population at a moderate cardiovascular risk.



Graph 1 - Relationship between increased left ventricular filling pressure and functional capacity.



Graph 2 - Relationship between left ventricular diastolic function and functional capacity. DF - diastolic function.

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Our study population was characterized as at a low cardiovascular risk; 62% of the individuals had a normal diastolic function, and 60% showed a low probability of CAD. Nonetheless, we could find correlations between diastole and exercise capacity.

In our protocol model, the number of patients with normal diastolic function was high, and the fact that the predominant diastolic dysfunction was relaxation abnormality (30% of the patients) may explain why the low functional capacity, but not the E/e' ratio, is associated with increased A wave velocity in conventional mitral Doppler. A wave velocity increases in patients with diastolic dysfunction with relaxation abnormality and becomes a significant parameter in a population with 30% of the patients classified in this degree of diastolic dysfunction.

Firstenberg et al's study²⁶ showed absence of correlation between E/e' ratio and left ventricular filling pressures in individuals without cardiovascular diseases, and this corroborates the findings of the present protocol, in which most of the patients did not present with cardiovascular disease (60%). The physiological basis for this lack of correlation may be reinforced by recent evidences that suggest that the early diastolic velocity of the septal annulus (e') is significantly influenced by the preload in normal ventricles, but this does not occur in ventricles with abnormal diastolic function, especially abnormalities in ventricular relaxation²⁷.

Advanced age was another independent factor related to low functional capacity. Decrease in functional capacity is evidenced as from 50 years of age, and becomes more evident after 75 years of age in both genders²⁸. In our study, the mean age of the individuals in the MET < 7 group was 62.1 years, thus corroborating the findings previously described. Multiple factors are related to this decreased functional capacity, such as decrease in joint motion, muscle mass, strength, coordination, and endurance, as well as the presence of chronic diseases^{28,29}.

Another clinical variable related to low functional capacity in our study was the female gender. The factors that explain this difference between genders are a reduced capacity of oxygen transportation, smaller muscle mass, higher percentage of fat, and lower cardiorespiratory fitness observed in women³⁰.

The major limitations of this study are its retrospective design; the use of only some parameters in the analysis of the diastolic function on echocardiogram; indirect assessment of physical capacity by exercise test instead of cardiopulmonary exercise test; and the fact that the interval between tests was 30 days at most. We should also mention that laboratory data and pulmonary functional capacity data were not available, since innumerable individuals were being followed-up in other services. However, the population studied is at a low risk for CAD and is representative of patients who undergo frequent assessments of the cardiovascular risk, which makes the parameters found useful in the clinical practice.

Conclusion

Diastolic dysfunction as determined by echocardiography, female gender, and age are associated with a lower exercise capacity in a population at a low risk for CAD with preserved left ventricular function.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.

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