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Treadmill exercise testing of asymptomatic men and women without evidence of heart disease

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Abstract

The aim of this study was to test the hypothesis of differences in performance including differences in ST-T wave changes between healthy men and women submitted to an exercise stress test. Two hundred (45.4%) men and 241 (54.6%) women (mean age: 38.7 ± 11.0 years) were submitted to an exercise stress test. Physiologic and electrocardiographic variables were compared by the Student *t*-test and the chi-square test. To test the hypothesis of differences in ST-segment changes, data were ranked with functional models based on weighted least squares. To evaluate the influence of gender and age on the diagnosis of ST-segment abnormality, a logistic model was adjusted; $P < 0.05$ was considered to be significant. Rate-pressure product, duration of exercise and estimated functional capacity were higher in men ($P < 0.05$). Sixteen (6.7%) women and 9 (4.5%) men demonstrated ST-segment upslope ≥0.15 mV or downslope ≥0.10 mV; the difference was not statistically significant. Age increase of one year added 4% to the chance of upsloping of segment ST ≥0.15 mV or downsloping of segment ST ≥0.1 mV ($P = 0.03$; risk ratio = 1.040, 95% confidence interval (CI) = 1.002-1.080). Heart rate recovery was higher in women ($P < 0.05$). The chance of women showing an increase of systolic blood pressure ≤30 mmHg was 85% higher ($P = 0.01$; risk ratio = 1.85, 95%CI = 1.1-3.05). No significant difference in the frequency of ST-T wave changes was observed between men and women. Other differences may be related to different physical conditioning.

Key words: ST-T wave changes; Exercise stress test; Asymptomatic; Women

Introduction

Physiologic and electrocardiographic variables of men and women submitted to exercise stress test are considered to differ (1-4). The poor predictive value of ischemic ST changes during exercise in women has been emphasized (1,4). For the interpretation of the tests in women it has been recommended to take into consideration a lower pre-test probability of disease in comparison to men (2,3) and a lower sensitivity of ST-segment changes for the diagnosis of myocardial ischemia (4).

Differences in sensitivity, specificity and diagnostic value of ST-segment and T wave changes have been reported (4,5). Furthermore, in the recovery after exercise, heart rate (6-8) and blood pressure (9,10) differences may also be present. These studies were performed in large series of patients and yielded relevant information. Nevertheless, we did not find recent studies comparing the exercise stress test of asymptomatic men and women without any evidence of heart disease after clinical examination.

We performed this study to evaluate variables of the exercise stress test in asymptomatic men and women without any evidence of heart disease after careful clinical and laboratory examination to test the hypothesis of differences in response between men and women. We were specifically interested in the comparison of ST-segment alterations between men and women.

Material and Methods

Study protocol

A cohort of asymptomatic individuals with no evidence of heart disease after careful clinical and laboratory examination was established to evaluate the exercise stress test. This cohort was established from 1998 onwards in a large General Outpatient Clinic of a tertiary care university hospital dedicated to cardiology that also provides primary and secondary levels of care. Asymptomatic individuals with

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normal clinical examination, as well as normal electrocardiogram and chest X-ray, were eligible and were invited to participate in the study. After informed written consent, participants volunteered and were submitted to further laboratory work-up including electrocardiographic exercise stress test, echocardiography, hemoglobin, hematocrit, leukocyte count, serum glucose, cholesterol, triglycerides, thyroid-stimulating hormone (TSH), and creatinine. Two-dimensional transthoracic echocardiography was performed according to a standard technique following published guidelines (11).

Inclusion criteria

Asymptomatic Brazilian men and women older than 18 years with a normal clinical examination, as well as normal electrocardiogram, chest X-ray, echocardiogram, and laboratory evaluation were included in the study.

Exclusion criteria

Individuals with symptoms of cardiovascular disease, systemic hypertension, *Trypanosoma cruzi* infection (Chagas' disease microorganism), diabetes mellitus, TSH <0.05 or >8 mg/dL, chronic obstructive pulmonary disease, asthma, renal failure, chronic inflammatory diseases, osteoarticular diseases, chronic anemia, neoplasia, and an abnormal electrocardiogram or chest X-ray were excluded from the study.

Study sample

A total of 441 individuals were studied, 200 (45.4%) men and 241 (54.6%) women, mean age 38.7 ± 11.0 years (range 18-74 years; Table 1). Seventy-eight participants were smokers, 37 of them (8.9%) men and 41 (10%) women. The baseline characteristics of the study sample are presented in Table 2.

Treadmill electrocardiographic exercise stress test. The test was performed on the Fukuda Denshi ML-8000 Star model (Japan) according to the Ellestad exercise protocol (12). Predicted peak heart rate was calculated as 220 - age. Individuals were encouraged to exercise until they experienced limiting symptoms, even if 85% of maximum predicted heart rate was achieved. During each exercise stage and recovery stage, symptoms, blood pressure, and heart rate were recorded. The criteria for interruption of the exercise were physical exhaustion or exceeded maximum heart rate predicted for the patient's age. Following peak exercise, individuals walked for a 3-min cool-down period at 1.5 mph without inclination. The ST-segment was measured 0.08 s after the J point in 3 consecutive QRS complexes with a flat baseline and R wave of equal amplitude. The amplitude of the R wave was measured in II, V_2 and V_5 leads and the Q wave in V_5 lead. Peak exercise capacity was estimated from treadmill time and reported as metabolic equivalents. Heart rate recovery was also measured and defined as maximum heart rate minus heart rate at 1 and 2 min after exercise with the subjects walking. To diagnose a normal treadmill electrocardiographic exercise stress test we followed previously published guidelines (13). Two physicians evaluated the electrocardiographic recordings of all tests independently in a blind fashion; disagreement was resolved by consensus.

Studied variables

The following variables were studied: a) demographic, clinical and laboratory variables: age, gender, smoking, body mass index, hemoglobin, serum glucose, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, left ventricle myocardial mass index, and left ventricular ejection fraction on echocardiography (11); b) variables of the treadmill exercise stress test - we studied heart rate, maximal ST-segment depression, R wave amplitude and Q wave amplitude, systolic and diastolic blood pressure, rate-pressure product (heart rate x systolic blood pressure), duration of exercise, and estimated exercise capacity (metabolic equivalents).

Statistical analysis

After descriptive statistics, continuous variables relative

Table 1. Age distribution of the men and women of the study sample.

Age (years)	Men	Women	Total
18 |- 29	46 (23%)	51 (21.2%)	97 (21.9%)
30 |- 39	54 (27%)	74 (30.7%)	128 (29.1%)
40 |- 49	72 (36%)	79 (32.8%)	151 (34.2%)
50 |- 59	22 (11%)	31 (12.8%)	53 (12.1%)
≥60	6 (3%)	6 (2.5%)	12 (2.7%)
Total	200	241	441

Data are reported as number with percent in parentheses.

Table 2. Demographic, clinical and laboratory characteristics of the men and women of the study sample.

Variables	Men		Women	
	N	Mean ± SD	N	Mean ± SD
Age (years)	200	39 ± 0.8	241	38.5 ± 0.7
Body mass index (kg/m^2)	188	26 ± 0.3	228	26 ± 0.3
Hemoglobin (g/dL)	189	15.2 ± 0.1	231	13.4 ± 0.1*
Creatinine (mg/dL)	189	0.98 ± 0.01	231	0.79 ± 0.01*
Glucose (mg/dL)	189	93.8 ± 1.6	231	89.9 ± 0.7*
Total cholesterol (mg/dL)	190	193.7 ± 2.7	231	187.9 ± 2.1
LDL cholesterol (mg/dL)	190	121.6 ± 2.5	231	117.3 ± 2.0
HDL cholesterol (mg/dL)	190	43.3 ± 1.3	231	50.9 ± 0.9*
Triglycerides (mg/dL)	190	135.8 ± 5.2	231	95.2 ± 3.5*

*P < 0.05 compared to men (Student *t*-test).

to gender were compared with the Student *t*-test and categorical variables relative to gender were compared using the chi-square test. To test the hypothesis of a sex-related difference regarding ST-segment in leads II, V_2 and V_5, data were ranked with functional models based on weighted least squares and submitted to categorical data analysis using the SAS System (14) and categorical data analysis (15). A logistic model was adjusted to evaluate the influence of gender and age on the diagnosis of ST-segment abnormality. A P value <0.05 was considered to be significant.

Ethics

The study was approved by the Ethics Committee of Human Research of the Hospital and all participants gave written informed consent.

Results

Baseline clinical characteristics of the study sample

Serum HDL cholesterol was higher in women. Hemoglobin, serum creatinine, triglycerides, glucose, and left ventricle mass index on echocardiography were higher in men. Other baseline clinical characteristics studied did not reveal statistically significant differences between men and women (Tables 2 and 3).

Table 3. Echocardiogram characteristics of the men and women of the study sample.

Variables	Men		Women	
	N	Mean ± SD	N	Mean ± SD
Left ventricular ejection fraction (%)	187	72.0 ± 0.2	228	72.0 ± 0.3
Left ventricle mass index (g/m^2)	179	78.2 ± 1	220	70.1 ± 0.8*

*P < 0.05 compared to men (Student *t*-test).

Treadmill electrocardiographic exercise stress test

a) *Heart rate*: 222 (92.1%) women and 186 (93%) men reached 85% of age-predicted peak exercise heart rate. Heart rate recovery in the 1st and 2nd min after exercise was faster in women (Table 4). A non-significant trend for a decrease in the heart rate recovery with increasing age for men and women was apparent (Figure 1).

Nine (3.7%) women and 13 (6.5%) men demonstrated heart rate recovery in the 1st min of recovery <12 bpm. An age increase of one year was associated with a 6% increase in risk of heart rate recovery <12 bpm in the 1st min of recovery (P = 0.005; risk ratio = 1.06; 95% confidence interval (CI) = 1.02-1.1). At the 2nd min of recovery, two (1%) women and four (2%) men demonstrated heart rate recovery <22 bpm. There was no influence of age or gender on the 2nd min of heart rate recovery.

b) *ST-segment*: Upslope morphology of the ST-segment and magnitude <0.1 mV were observed in 225 (93.3%) women and in 191 (95.5%) men. Sixteen (6.7%) women and 9 (4.5%) men demonstrated ST-segment upslope ≥0.15 mV or downslope ≥0.1 mV. This finding was more frequent in lead II (5.44%), followed by lead V_5 (2.73%) and lead V_2 (0.23%; II *vs* V_2, P < 0.0001; II *vs* V_5, P = 0.001; V_2 *vs* V_5, P = 0.02). An age increase of 1 year increased by 4% (P = 0.03; risk ratio = 1.040, 95%CI = 1.002-1.080) the chance of upsloping of segment ST ≥0.15 mV or downsloping of segment ST ≥0.1 mV. The difference was not significant relative to sex.

c) *R and Q wave amplitude*: There was a trend to a

Table 4. Treadmill electrocardiographic exercise stress test characteristics of the men and women of the study sample.

Variables	Men		Women	
	N	Mean ± SD	N	Mean ± SD
Baseline heart rate (bpm)	200	77.9 ± 0.9	241	82.9 ± 0.8*
Peak exercise heart rate (bpm)	200	171.5 ± 1	241	170.1 ± 0.9
Heart rate recovery 1st min (bpm)	155	143.5 ± 1.1	207	139.2 ± 1.3*
Heart rate recovery 2nd min (bpm)	180	123.2 ± 1.1	216	117.2 ± 1.2*
Baseline systolic blood pressure (mmHg)	200	124.5 ± 0.7	241	119.5 ± 0.7*
Peak exercise systolic blood pressure (mmHg)	200	181.0 ± 1.6	241	166.8 ± 1.7*
Baseline diastolic blood pressure (mmHg)	200	78.7 ± 0.6	241	77.1 ± 0.6
Peak exercise diastolic blood pressure (mmHg)	200	84.2 ± 0.9	241	81.5 ± 0.8*
Rate-pressure product (bpm x mmHg)	200	31023.6 ± 321.7	241	28378.7 ± 313.1*
Exercise duration (min)	200	8.4 ± 0.1	241	6.9 ± 0.1*
Exercise capacity (MET)	188	12.7 ± 0.2	228	10.4 ± 0.2*

MET = metabolic equivalent. *P < 0.05 compared to men (Student *t*-test).

decrease in R wave amplitude and to an increase in Q wave at peak exercise relative to baseline values for both genders.

The decrease in R wave amplitude at peak of exercise in leads V_2 and V_5, the sum of R wave's amplitude in leads II, V_2 and V_5 were higher in men (Table 5).

The normal decrease in R wave amplitude at peak exercise was more apparent with the sum of leads II, V_2 and V_5 (observed in 342 participants) than R wave amplitude measured in the V_5 lead (observed in 283 participants).

Among 8 patients with ST-segment downsloping in lead V_5, three patients demonstrated a diminished Q wave in lead V_5 at peak exercise.

d) *Blood pressure*: Baseline mean systolic blood pressure, peak exercise systolic and diastolic blood pressure and differences between peak exercise and baseline systolic blood pressure were higher in men (Tables 4 and 5).

An increase of systolic blood pressure ≤30 mmHg was observed in 56 (23.2%) women and 28 (14%) men. The chance of women to show an increase of systolic blood pressure ≤30 mmHg was 85% higher than men (P = 0.01; risk ratio = 1.85, 95%CI = 1.1-3.05).

e) *Rate-pressure product*: The rate-pressure product was higher in men (Table 4). A rate-pressure product <30.0 bpm·mmHg^{-1}·$(10^{-3})^{-1}$ was observed in 159 (65.9%) women and in 81 (40.5%) men. The chance of a rate-pressure product <30.0 bpm·mmHg^{-1}·$(10^{-3})^{-1}$ for women was almost three times higher than for men (P = 0.001; risk ratio = 2.96, 95%CI = 2.0-4.39). For an age increase of 1 year, the chance of a rate-pressure product <30.0 bpm·mmHg^{-1}·$(10^{-3})^{-1}$ increased 3% (P = 0.002; risk ratio = 1.03, 95%CI = 1.01-1.05).

f) *Estimated exercise capacity*: Exercise duration and estimated exercise capacity were higher in men (Table 4). A trend to a decrease in estimated exercise capacity with increasing age was verified for men and women up to 59 years of age (Figure 2).

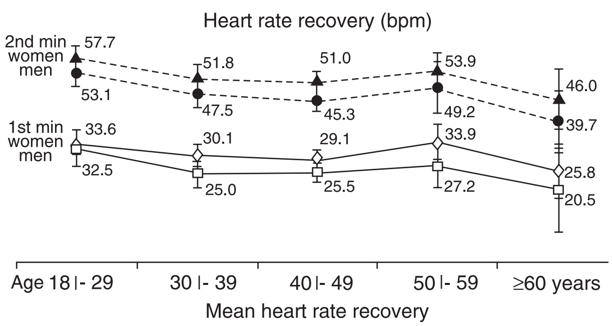

Figure 1. Mean heart rate recovery in the 1st and 2nd min after exercise relative to age and gender. (Student *t*-test).

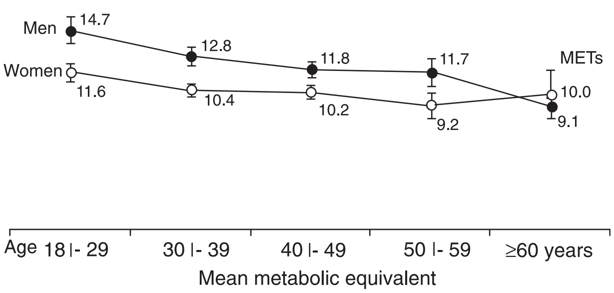

Figure 2. Mean of estimated exercise capacity in metabolic equivalents (METs) during treadmill exercise stress testing relative to age and gender. (Student *t*-test).

Table 5. Differences between baseline and peak exercise in blood pressure, R wave amplitude and Q wave amplitude in men and women.

Variables	Men (N = 200)	Women (N = 241)
Systolic blood pressure (mmHg)	56.5 ± 1.6	47.3 ± 1.6*
Diastolic blood pressure (mmHg)	5.5 ± 0.8	4.4 ± 0.7
R wave in II (mm)	-2.7 ± 0.2	-2.2 ± 0.2
R wave in V_2 (mm)	-1.4 ± 0.1	-0.8 ± 0.1*
R wave in V_5 (mm)	-2.1 ± 0.1	-1.3 ± 0.2*
R wave (II + V_2 + V_5) (mm)	-6.2 ± 0.4	-4.3 ± 0.3*
Q wave in V_5 (mm)	0.5 ± 0.0	0.4 ± 0.0

Data are reported as means ± SD. *P < 0.05 compared to men (Student *t*-test).

Discussion

We observed statistically significant differences between healthy men and women after the beginning of the electrocardiographic exercise stress test for peak exercise systolic blood pressure and diastolic blood pressure, rate-pressure product, R wave amplitude, exercise duration, and estimated exercise capacity. During recovery after exercise, differences were significant for heart rate recovery in the 1st and 2nd min after exercise. In contrast, we did not observe significant differences in the treadmill electrocardiographic exercise stress test between men and women for ST-segment, for peak exercise heart rate or Q wave amplitude.

Heart rate recovery was faster in women and this difference persisted, though not statistically significant, from the 3rd to the 7th decade of age. This finding raises the question of whether the mechanism of parasympathetic reactivation after exercise may be more pronounced in women. In a previous study, there was no significant correlation between heart rate recovery and autonomic function evaluated by heart rate variability during the 1st and 2nd min after exercise.

The SDNN, SDANN, SDNNi, rMSSD, and pNN50 indices were correlated significantly with heart rate recovery only at the 3rd and 4th min of recovery (16).

Fewer women (3.7%) than men (6.5%) showed a heart rate recovery after exercise below 12 bpm and the probability of this finding increased with age. This was an interesting finding in the absence of any evidence of heart disease since previous studies have rated 12 bpm as a marker of less favorable prognosis (6,17).

We observed an ST-segment upslope ≥0.15 mV or downslope ≥0.1 mV in 16 (6.7%) women and 9 (4.5%) men, lower than the range of 14 to 67% of previously reported cases (12). This lower frequency may have been related to the criteria used for enrollment in the present study, namely asymptomatic subjects with normal clinic examination, baseline electrocardiogram, chest X-ray, and echocardiogram.

In the present series, ST-segment upslope ≥0.15 mV or downslope ≥0.1 mV was observed more frequently in lead II. In patients with a normal resting electrocardiogram, exercise-induced ST-segment depression confined to the inferior leads is of little value for the identification of coronary disease (12,18).

We did not observe significant differences between men and women in ST-segment during the treadmill electrocardiographic exercise stress test. This observation contrasts with the long held view in clinical practice that ST abnormalities may be more frequent in women than in men (4,12).

The normal decrease in R wave amplitude at peak exercise was more apparent with the sum of leads II, V_2 and V_5 (observed in 342/441 participants, 76%) than the R wave amplitude measure in V_5 lead (observed in 283/441 participants, 64%). This finding suggests that R wave amplitude may be better analyzed in leads II, V_2 and V_5, and not in a single lead. Other investigators have shown that R wave amplitude in the lateral precordial leads usually decreases more in healthy subjects than in patients and a significant correlation with left ventricular function has been demonstrated (12,19-22).

Most patients demonstrated an increase in Q wave amplitude at peak exercise, as shown in previous studies (23,24). However, among 8 patients with ST-segment downsloping in lead V_5, three demonstrated a diminished Q wave in lead V_5 at peak exercise. This finding was unexpected in this setting; whether it means an abnormal result remains to be established.

Baseline mean systolic blood pressure and peak exercise systolic and diastolic blood pressure were higher in men, as also observed by others (13,25,26). This finding in women may be attributed to their smaller muscle mass, lower hemoglobin and blood volume, and smaller stroke volume compared with men.

It is noteworthy that an increase of systolic blood pressure ≤30 mmHg was observed in 23.2% of women and 14% of men. The chance of women showing an increase of systolic blood pressure ≤30 mmHg is 85% higher than in men. Thus, this finding may be detected in otherwise healthy individuals, and may be ascribed to poor physical conditioning.

We observed influence of gender and age on the rate-pressure product. The chance of a rate-pressure product <30 $bpm \cdot mmHg^{-1} \cdot (10^{-3})^{-1}$ for women was almost three times higher than for men and, for an age increase of one year, the chance of a rate-pressure product <30 $bpm.mmHg^{-1}.(10^{-3})^{-1}$ increased by 3%. This was an expected finding since the rate-pressure product depends on both systolic blood pressure and heart rate.

Functional capacity was higher in men than in women and tended to decrease with age for both genders, as also observed by others (27,28). Maximal aerobic capacity declines 8 to 10% per decade in sedentary men and women (27). In the present study, this decline was observed in the second, third, fourth, and sixth decade for men and in the third and fifth decade for women, a trend similar to that observed in other studies (27,28).

The present study has limitations. The sample was recruited from asymptomatic volunteers with normal clinical and laboratory examination and may not be representative of the whole population. Few individuals were older than 60 years of age and elderly subjects were under-represented. Additionally, further invasive diagnostic work-up was not recommended to the participants.

We were not able to demonstrate differences in the frequency of ST-segment changes in men and women submitted to an electrocardiographic exercise stress test. Our findings for this study sample do not support the previously suggested contention of different frequencies of ST-T wave changes in men and women. Other differences observed between men and women were more subtle and may have been related to different physical conditioning.

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