

Assessment of Myocardial Ischemia in Obese Individuals Undergoing Physical Stress Echocardiography (PSE)

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Abstract

Background: Physical stress echocardiography is an established methodology for diagnosis and risk stratification of coronary artery disease in patients with physical capacity. In obese (body mass index ≥ 30 kg/m²) the usefulness of pharmacological stress echocardiography has been demonstrated; however, has not been reported the use of physical stress echocardiography in this growing population group.

Objective: To assess the frequency of myocardial ischemia in obese and non-obese patients undergoing physical stress echocardiography and compare their clinical and echocardiographic differences.

Methods: 4,050 patients who underwent treadmill physical stress echocardiography were studied according to the Bruce protocol, divided into two groups: obese (n = 945; 23.3%) and non-obese (n = 3,105; 76.6%).

Results: There was no difference regarding gender. Obese patients were younger (55.4 ± 10.9 vs. 57.56 ± 11.67) and had a higher frequency of hypertension (75.2% vs. 57.2%; $p < 0.0001$), diabetes mellitus (15.2% vs. 10.9%; $p < 0.0001$), dyslipidemia (59.5% vs 51.9%; $p < 0.0001$), family history of coronary artery disease (59.3% vs. 55.1%; $p = 0.023$) and physical inactivity (71.4% vs. 52.9%, $p < 0.0001$). The obese had greater aortic dimensions (3.27 vs. 3.14 cm; $p < 0.0001$), left atrium (3.97 vs. 3.72 cm; $p < 0.0001$) and the relative thickness of the ventricle (33.7 vs. 32.8 cm; $p < 0.0001$). Regarding the presence of myocardial ischemia, there was no difference between groups (19% vs. 17.9%; $p = 0.41$). In adjusted logistic regression, the presence of myocardial ischemia remained independently associated with age, female gender, diabetes and hypertension.

Conclusion: Obesity did not behave as a predictor of the presence of ischemia and the physical stress echocardiography. The application of this assessment tool in large scale sample demonstrates the feasibility of the methodology, also in obese. (Arq Bras Cardiol. 2015; 104(5):394-400)

Keywords: Myocardial Ischemia; Obesity; Echocardiography, Stress / methods; Coronary Artery Disease / mortality.

Introduction

Coronary artery disease (CAD) is currently the leading cause of mortality in Brazil, contributing to over 30% of deaths and has substantial impact on health care expenditures¹⁻⁵.

The disease is caused by independent risk factors, such as systemic arterial hypertension (SAH), diabetes mellitus (DM), dyslipidemia and smoking. Obesity, a clinical condition that has extensively increased in Brazil, is considered a conditional risk factor in some publications, whereas others consider it an independent risk factor for CAD⁶⁻¹⁵. There is also

epidemiological evidence that confers a protective or, at least a neutral role to obesity in patients with cardiovascular disease, which constitutes the paradox of obesity¹⁵⁻¹⁷.

Obesity is characterized by the excess of adipose tissue, associated with several comorbidities. Among these are coronary atherosclerosis, which comprises a series of inflammatory responses at cellular and molecular level, of which reactions are further exacerbated in obese patients^{18,19}. Physical stress echocardiography has been widely used in the noninvasive investigation of the CAD²⁰. Physical exertion is the triggering agent of cardiovascular stress of choice for individuals with preserved physical capacity, as it results in greater increase in inotropism and provides physiological information about the presence, location and extent of ischemia^{21,22}. Some studies have demonstrated the feasibility, safety and diagnostic usefulness of pharmacological stress echocardiography in obese individuals^{23,24}. Nevertheless, the use of physical stress echocardiography (PSE) in obese individuals has been rarely reported in the literature, perhaps due to the assumption that this population would not be

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Manuscript received July 20, 2013, revised November 4, 2014, accepted November 21, 2014.

DOI: 10.5935/abc.20150006

able to exercise enough to achieve proper heart rate for the method to be carried out.

In this study we speculate about the capacity of PSE to diagnose CAD in obese patients with preserved physical capacity. Therefore, the aim of this research is to verify the frequency of myocardial ischemia in obese and non-obese patients submitted to PSE and compare the clinical and echocardiographic differences.

Methods

Patients

Between January 2000 and January 2012 8751 volunteers of both genders, with suspected or established CAD were included in the study. All subjects underwent, as recommended by their physicians, PSE on Hospital São Lucas Echocardiography Service (ECOLAB), considered a cardiology center of reference in the state of Sergipe, Brazil, which has accreditation level three (Qualisa IQG-Instituto Qualisa de Gestão). Data from these patients, and the results of their examinations were standardized and stored in a digital database.

The following exclusion criteria were used: refusal to participate in the study, patients with duplicate data in the database records (in patients who underwent annual tests, we selected the most recent one) and inappropriate indications of the examination (young patients with no risk factors for coronary atherosclerosis and no alterations in the clinical examination and resting electrocardiogram). Only 7 patients from the obese group could not undergo the examination, due to technical difficulties. Therefore, there were 4050 patients with suspected or established CAD, who were divided in two groups: (G1) obese (n = 945) and (G2) non-obese patients (n = 3105).

Dyslipidemia is characterized by the presence of serum levels (after 12-hour fasting) of total cholesterol > 200 mg/dL and/or triglycerides > 150 mg/dL or the use of lipid-lowering drugs (statins and/or fibrates). Diabetes mellitus was defined as fasting glucose levels > 126 mg/dL or the use of insulin or oral hypoglycemic agents.

The isolated or combined indications for PSE were: evaluation of chest pain; preoperative evaluation for non-cardiac surgery; presence of positive exercise test (ET) for myocardial ischemia in patients at low risk for CAD; Negative ET for myocardial ischemia in patients with intermediate risk of CAD; onset of arrhythmia during ET; previously established CAD stratification and post-acute coronary syndrome risk stratification.

The ethical principles that guide human experimentation were followed, and all patients signed an informed consent form. The study was approved by the Research Ethics Committee of the Federal University of Sergipe (CAAE - 0121.0.107.000-09).

Examination Protocol

The echocardiographic assessment was performed in all study participants, following the classically described

technical aspects²⁵. The Bruce protocol was used to carry out the exercise tests. The test was interrupted at the onset of the following symptoms and/or signs: chest pain, dyspnea, muscle fatigue, SAH (BP \geq 240 x 120 mmHg), arterial hypotension (non-elevation of BP during the ET or its decrease), pre-syncope and severe arrhythmias (ventricular fibrillation and ventricular tachycardia). During the test, the individuals were continuously monitored by three-lead ECG. Heart rate was monitored continuously and patients encouraged to exceed 85% of maximum heart rate for age were considered negative for myocardial ischemia. The exercise test load was expressed in metabolic equivalents (METs). The ET was considered positive for myocardial ischemia when a decrease in the ST-segment \geq 1 mm for men and \geq 1.5 mm for women was observed at 0.08 seconds beyond J point²².

Echocardiographic recordings were carried out with Hewlett-Packard/Phillips SONOS 5500 equipment, using a 2.5-MHz transducer also from Hewlett-Packard/Phillips. Two-dimensional echocardiographic images were obtained and recorded with the patient in the left decubitus position at 45° (or adequate obliquity to obtain satisfactory echocardiographic images) in the parasternal (longitudinal and transverse) and apical acoustic windows (two and four-chamber) during rest, immediately after the exercise, while HR was still high, and in the recovery period.

Segmental motion was evaluated by the same experienced, level-III echocardiographer, as recommended by the American Society of Echocardiography²⁶. The segmental parietal thickening of the LV was quantitatively assessed at rest and after exercise using the 16-segment model and classified as: 1 (normal), 2 (hypokinetic), 3 (akinetic) and 4 (dyskinetic). The left ventricular wall motion score index (LVWMSI) was obtained by adding the scores of each segment and dividing the value found for 16, the total number of LV segments. The development of stress-induced wall motion abnormalities was considered an indicator of myocardial ischemia.

Test interpretation

Both scanned and printed images were used for interpretation and report, immediately after the examination, by a single echocardiographer aware of the clinical conditions and previous history of the patient.

The calculation of left ventricular wall motion score index (LVWMSI) was carried out using the standardized score by the American Society of Echocardiography²⁶, which attributes to each of the 16 segments the following values: 1 (normal); 2 (hypokinetic); 3 (akinetic) and 4 (dyskinetic). The LVWMSI was obtained by adding the values obtained for each of the 16 segments divided by the number of studied segments.

The myocardial motion score index 1 (normal) was obtained by adding the score of each visualized segment and dividing the value obtained by 16 (number of left ventricular segments). This evaluation was performed at rest and after exercising. The ventricular wall contractility was studied based on the LVWMSI: 1 = Normal; Mild Ventricular Dysfunction = 1.1-1.6; Moderate Ventricular Dysfunction = 1.61 to 2.0; Severe Ventricular Dysfunction \geq 2.0.

The physical stress echocardiographic assessment was defined as abnormal when in the presence of ischemic PSE, i.e., LVWMSI > 1 at rest and/or under stress.

Statistical Analysis

Quantitative variables were described as mean and standard deviation (SD). The Kolmogorov-Smirnov test was used to evaluate normality of the studied sample. Then Student's *t* test or Mann-Whitney was used for independent groups, according to the sample normality pattern. As for categorical variables, absolute frequency and percentages were used. To compare characteristics of categorical variables between the two groups, the chi-square test or Fisher's exact test was used, as appropriate. Logistic regression analysis was performed, of which outcomes were the presence of ischemia in PSE, adjusting for the variables: age, gender, diabetes mellitus, dyslipidemia, SAH, sedentary lifestyle and family history. The hazard ratios, accompanied by 95% confidence intervals, were shown. The BioEstat software, version 5.0 was used to perform statistical calculations and logistic regression was carried out using Stata, version 13.0. A two-tailed *p* value < 0.05 was considered statistically significant for all tests.

Results

Of 4050 patients that underwent PSE in the 12-year period (2000-2012), 945 obese individuals were analyzed and compared with 3105 non-obese ones. Individuals with BMI ≥ 30 kg/m² were considered obese, which corresponded to 23.3% of the total sample. There were no differences regarding gender, but obese individuals were younger (55.4 ± 10.9 years vs 57.6 ± 11.7 years; *p* < 0.0001), as shown in Table 1.

As for cardiovascular risk factors, obese individuals had significantly (*p* < 0.0001) higher incidence of hypertension, diabetes mellitus, dyslipidemia, family history of CAD and physical inactivity (Table 1). In the adjusted logistic regression analysis, myocardial ischemia remained independently

associated to age, dyslipidemia, female gender, diabetes mellitus and hypertension (Table 2).

Among the previous symptoms that motivated the examination indication, the obese individuals had more atypical chest pain (49.4%) and dyspnea (7.5%). During the examination, the presence of simple arrhythmia (isolated extrasystoles) prevailed in the non-obese group (Table 3).

Regarding the heart rates achieved by the two groups, we observed that 251 obese individuals (26.6%) reached HR above the maximum value, which shows that some obese individuals have enough physical capacity to achieve high values of HR at the PSE (Table 4).

The analysis of the echocardiographic characteristics showed a significant difference (*p* < 0.0001) in the size of the aorta, left atrium, left atrial volume and relative thickness of the left ventricle (LV). However, it was observed that there was no difference regarding left ventricular ejection fraction (*p* = 0.5), E/e' ratio (*p* = 0.5), LVMI at rest (*p* = 0.4) and LVMI at effort (*p* = 0.6), as shown in table 5.

Regarding the occurrence of myocardial ischemia, the frequency, in the total sample, was 18.1% CI (17.0 to 19.3), and both groups showed homogeneous behavior (Figure 1).

Discussion

This study showed that PSE, an established methodology for diagnosis and risk stratification of CAD, can be used in myocardial ischemia assessment in obese patients with physical capacity to perform the test on a treadmill with no complications.

Therefore, as it is a first-choice test for inducing ischemia in patients with preserved physical exercise capacity²⁵, the exercise test can be incorporated in clinical practice also for the evaluation of the obese patients.

Although lower exercise tolerance in obese individuals has been described²⁶, we could not identify, in this study, differences between the groups regarding the occurrence of myocardial ischemia on PSE: 19% in the obese and 17.9% in the non-obese patients.

Table 1 – Clinical characteristics of obese and non-obese patients submitted to PSE

Variable	Obese (n = 945)	Non-obese (n = 3105)	p
Age (years)*	55.4 ± 10.9	57.6 ± 11.7	< 0.001
Female gender	492 (52.1%)	1637 (52.7%)	0.738
Hypertension	711 (75.2%)	1775 (57.2%)	< 0.001
Dyslipidemia	562 (59.5%)	1612 (51.9%)	< 0.001
Diabetes mellitus	144 (15.2%)	338 (10.9%)	< 0.001
Family history of DAC	560 (59.3%)	1710 (55.1%)	0.023
Waist circumference (cm)	108 ± 12.7	91.7 ± 9.95	< 0.001
Sedentary life style	675 (71.4%)	1644 (52.9%)	< 0.001
Smoking	46 (4.9%)	135 (4.3%)	0.50
Previous infarction	39 (4.1%)	118 (3.8%)	0.63

* Values expressed as mean and standard deviation. PSE: physical stress echocardiography.

Table 2 – Results of the logistic regression between risk factors for CAD, with the outcome variable myocardial ischemia

Variable	Adjusted OR	CI (95%)	p
Dyslipidemia	2.02	1.69-2.42	< 0.001
Family history	1.55	1.30-1.84	< 0.001
Diabetes mellitus	1.54	1.23-1.92	< 0.001
Hypertension	1.45	1.20-1.76	< 0.001
Age (years)	1.03	1.02-1.04	< 0.001
Obesity	1.01	0.83-1.24	0.877
Female gender	1.82	1.54-2.15	< 0.001

Table 3 – Previous symptoms for physical stress echocardiography indication

Variable	Obese (n = 945)	Non-obese (n = 3105)	p
Asymptomatic	347 (36.7%)	1442 (36.8%)	0.97
Typical chest pain	55 (5.82%)	179 (5.76%)	0.95
Atypical chest pain	467 (49.4%)	1332 (42.9%)	< 0.001
Dyspnea	71 (7.5%)	143 (4.6%)	< 0.001
Simple arrhythmia	253 (26.8%)	871 (28.1%)	0.44

Table 4 – Heart rates achieved by obese and non-obese individuals during PSE

Variable	Obese (n = 945)	Non-obese (n = 3105)	p
HR < submaximal value	110 (11.6%)	230 (7.4%)	< 0.001
Submaximal HR	431 (45.6%)	1064 (34.3%)	< 0.001
Maximal HR	154 (16.3%)	590 (19%)	0.06
HR > maximum value	251 (26.6%)	1219(39.3%)	< 0.001

Table 5 – Echocardiographic characteristics of obese and non-obese patients submitted to PSE

Variable	Obese (n = 945)	Non-obese (n = 3105)	p
Aorta (cm)	3.27 ± 0.41	3.14 ± 0.39	< 0.001
Left atrium (cm)	3.97 ± 0.43	3.72 ± 0.43	< 0.001
Ejection fraction	0.66 ± 0.06	0.70 ± 1.79	0.506
LA volume index	23.65 ± 8.95	21.50 ± 7.75	< 0.001
LV relative thickness	33.76 ± 5.31	32.80 ± 5.16	< 0.001
LV mass index	90.88 ± 29.12	85.92 ± 22.50	< 0.001
E/e' ratio	8.95 ± 2.88	8.72 ± 3.06	0.510
LVWMSI at rest	1.01 ± 0.076	1.01 ± 0.089	0.46
LVWMSI at exercise	1.02 ± 0.091	1.02 ± 0.097	0.65

LVWMSI: left ventricular wall motion score index. I/E': ratio between the E-wave velocity obtained by conventional Doppler and e'-wave velocity, obtained by tissue Doppler; LA: left atrium; LV: left ventricle; HR: heart rate; PSE: physical stress echocardiography.

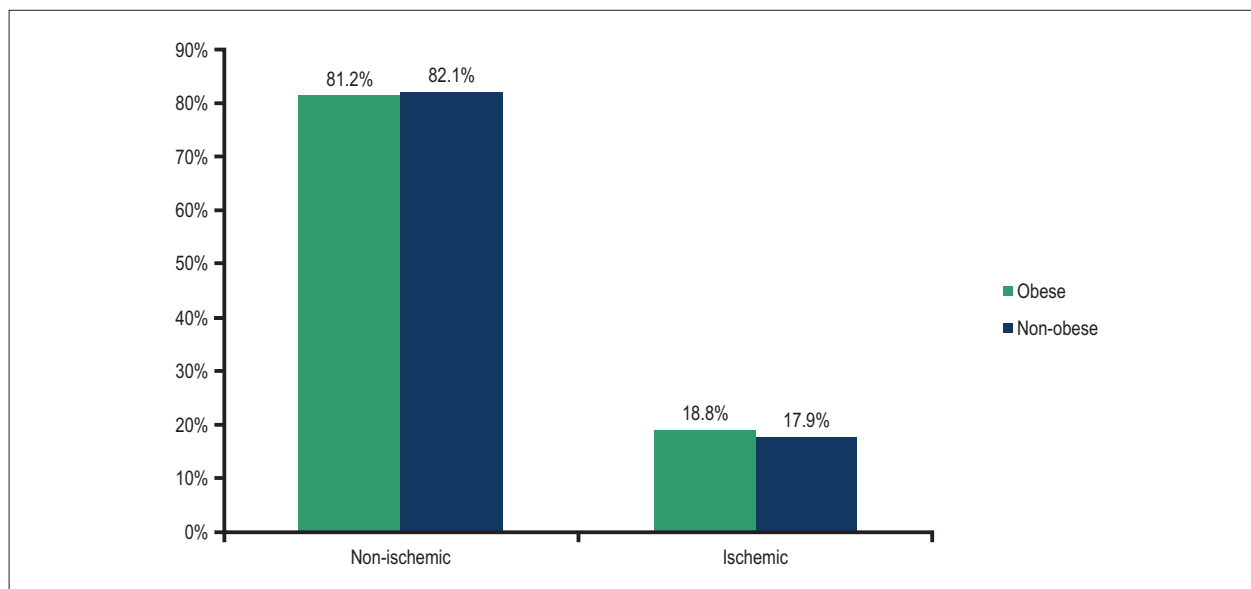


Figure 1 – Comparison of the frequency of myocardial ischemia on PSE between the obese and non-obese groups.

Several published studies have shown a protective effect of obesity, according to BMI, in patients undergoing percutaneous coronary intervention (PCI)²⁷. In the CADILLAC study, Nikolski et al²⁷ found an association between high BMI and lower mortality. The "obesity paradox" has also been observed in patients undergoing coronary artery bypass surgery and in patients with congestive heart failure. It is believed that this protection occurs by the presence of higher coronary diameters and lower age-range groups observed in obese populations, and even the excessive use of anticoagulants in this população²⁸⁻³⁰.

There is a scarcity in the medical literature of studies on stress echo in obese individuals; the few existing studies used only pharmacological stress.

To the best of our knowledge, this is the first Brazilian study using PSE in obese patients. Further studies are required to validate the results of this study in order to expand the use of this methodology in CAD assessment in obese individuals.

The PSE has similar accuracy to the pharmacological test, with the advantage of its lower cost, a fact that certainly has importance considering the low purchasing power of the majority of Brazilian population³¹⁻³⁵.

This study had the following limitations: (a) patients were selected at a single center, which does not belong to the reference system of the Brazilian Unified Health System (SUS) for PSE performance, which indirectly led to a larger sample differencing in relation to the target population; (b) it is a registry with non-probability sampling; (c) patients were not stratified into fixed and induced ischemia, which identifies those with established CAD; (d) obesity was not classified in degrees of severity, thus not allowing the evaluation of ischemia in the obese subgroups.

The large sample volume, however, gives reliability to the results. It would be interesting to carry out studies to address the use of this methodology in obese patients with different degrees of obesity and compare the results with those of the pharmacological testing for further consolidation of its clinical use.

Conclusion

The findings of the present study show that there was no difference between the groups regarding the frequency and predictors of myocardial ischemia, demonstrating the feasibility of this methodology in obese individuals.

Author contributions

Conception and design of the research: Silveira MGM, Oliveira JLM. Acquisition of data: Silveira MGM, Sousa ACS, Santos MAA, Tavares IS, Andrade SM, Melo LD, Andrade LSO, Santos ELA, Oliveira JLM. Analysis and interpretation of the data: Silveira MGM, Sousa ACS, Santos MAA, Andrade SM, Melo LD, Oliveira JLM. Statistical analysis: Silveira MGM, Melo LD, Santos MAA. Writing of the manuscript: Silveira MGM, Sousa ACS, Santos MAA, Oliveira JLM. Critical revision of the manuscript for intellectual content: Silveira MGM, Sousa ACS, Santos MAA, Tavares IS, Andrade SM, Melo LD, Oliveira JLM, Andrade LSO, Santos ELA. Supervision / as principal investigator: Silveira MGM, Sousa ACS, Oliveira JLM.

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 article is part of the course conclusion work submitted by Mara Grazielle Maciel Silveira, from Universidade Federal de Sergipe.

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