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RESEARCH ARTICLE

False Positive Results on Dobutamine Stress Echocardiography: A New Marker of Risk for Ischemic Events

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ABSTRACT

Background: Although dobutamine stress echocardiography (DSE) has a high specificity, there is still a subset of patients with false positive tests (FP); whether these results have prognostic value remains unclear.

Aims: To identify the clinical and echocardiographic predictors of FP on DSE and to evaluate the prognostic impact of FP on DSE.

Methods: Retrospective study of 355 consecutive patients who underwent DSE for ischemia assessment over a one-year period: 134 (37,7%) women, 70,3 ± 0,57 years. Demographics, risk factors, clinical and laboratorial parameters and DSE variables were evaluated. Patients were divided into 2 groups regarding the presence (FP+) or the absence (FP0) of a FP result on DSE and a comparative analysis was performed to characterize the groups and identify potencial predictors of FP results. Patients were followed for 2 years to assess acute myocardial infarction, hospitalization for acute heart failure (HF) and mortality.

Results: The FP rate was 4,5%. Comparing to FP0, patients in group FP+ were younger, baseline wall motion abnormalities were more frequent, had higher mean blood pressure values at rest and at peak stage and more often hypertensive response. There were no significant differences regarding previous coronary artery disease, medication or complete left bundle branch block. By multivariate analysis, only mean blood pressure values at rest (OR 0,01; 95%CI 0,005-0,02; p=0,003) and at peak stage (OR 0,02; 95%CI 0,000-0,004; p=0,003) were independent predictors of FP. During follow-up was observed: acute myocardial infarction (FP+: 12,5% vs FP0: 1,8%, p=0,046), HF (FP+: 6,3% vs FP0: 11,5%, p=0,44) and mortality (FP+: 6,3% vs FP0: 6,2%, p=0,65). After adjustment for age, sex and comorbidities, there were no diferences between the groups regarding HF and mortality, but the group FP+ mantained a higher rate of acute myocardial infarction (OR 0,21; 95%CI 0,065-0,354; p=0,005).

Conclusion: A FP result on DSE was associated with higher mean blood pressure values during the test and with higher rates of acute myocardial infarction during follow-up. This result on DSE should therefore be faced as a risk marker for ischemic events and can identify patients that may benefit from aggressive risk factor control and careful clinical follow-up.

Introduction

Dobutamine stress echocardiography (DSE) was introduced in the early 1980s and is a non-invasive test to assess ischemia that is often used when there is a high clinical probability of coronary artery disease, given its high sensitivity (95%) and specificity (78%)[1]. However, there is still a subgroup of patients with false positive results (FP) in DSE and their prognosis remains uncertain, with studies showing mortality similar to true positives.[2,3] This is corroborated by Rachwan et al., who reported that patients with FP results on stress echocardiography had similar all-cause mortality to those with true positives results, so they could benefit from aggressive risk factor control and careful clinical follow-up[2]. The study by From et al. found that 480 patients (32,5%) in a group of 1477 patients had FP results, and the outcomes of these patients, namely all-cause mortality, were similar to those of patients with true-positive results during an average follow-up period of 2,4 ± 1,0 years.[3] However these FP results are challenging as the best treatment for these patients in still unclear.

Prior studies have identified predictors of FP results in DSE, namely female gender[2,4,5], the absence of diabetes[2,4], the hypertensive response to exercise[4] and alterations in segmental contractility of the middle and apical segments of the left ventricle[4]. Qamruddin S. reported that an hypertensive response to exercise (defined as peak systolic blood pressure >210 mmHg in men and >190 mmHg in women) was considered to be one of the reasons for false-positive stress echocardiography, with 10% of the patients with abnormal stress echocardiography developed a hypertensive response to exercise, suggesting that a superior blood pressure control prior to stress echocardiography may prevent some false-positive tests.[4] Accounting for this factor could improve the interpretation of stress echocardiography results and potentially avoid unnecessary invasive coronariographies with a better selection of patients.

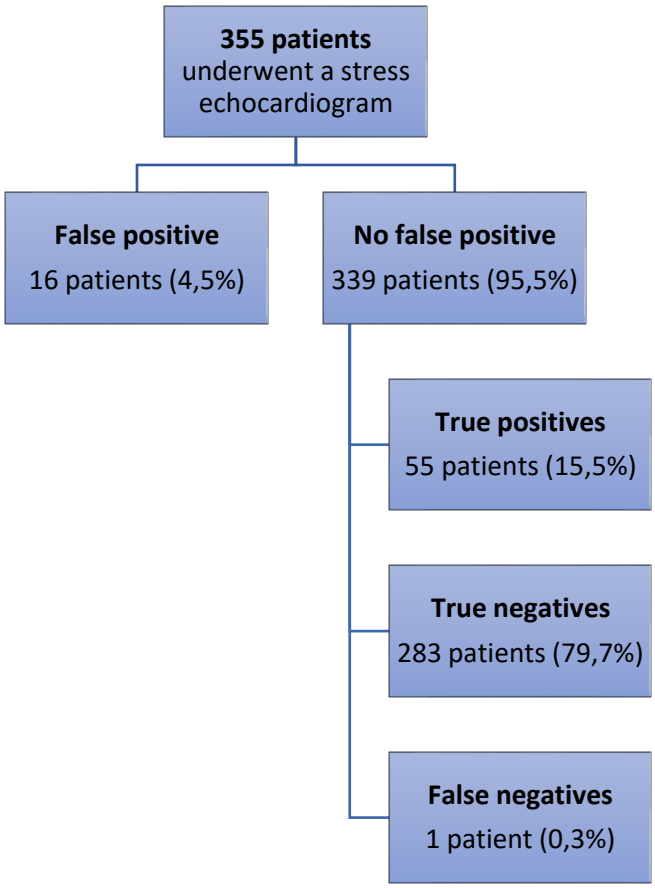
The purpose of this study was to identify the clinical and echocardiographic predictors of FP on DSE and to evaluate the prognostic impact of FP on DSE.

Methods

This was a retrospective observational study of 355 consecutive patients who underwent DSE for ischemia assessment at our center over a one-year period. This study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) with the requirement for informed consent being waived due to the retrospective nature of this study. Data regarding demographics (age, gender and mean body surface area), comorbidities (arterial hypertension, diabetes, dyslipidemia, smoking, obesity, chronic obstructive pulmonary disease, chronic renal failure, thyroid dysfunction, atrial fibrillation/atrial flutter, history of coronary artery disease and stroke/transient ischemic attack), usual medication (namely, beta blockers), laboratorial parameters (hemoglobin, hematocrit and creatinine value), baseline electrocardiographic (the presence of left bundle branch block) and rest echocardiographic (interventricular septum diastolic thickness, left ventricle diastolic diameter base, wall motion abnormality, wall motion score index and left ventricular ejection fraction) variables, were entered into a database. Left ventricular ejection fraction was determined by the Simpson method. Left ventricular wall motion score index (WMSI) was calculated by adding the score of each segment and dividing the total sum by the number of visualized segments. Segments were graded based on systolic thickening and excursion: 1 = normal; 2 = hypokinetic; 3 = akinetic; and 4 = dyskinetic. Cardiac catheterization with coronary angiography was performed using standard clinical techniques and all angiographic studies were interpreted by highly trained observers. A FP result was defined as a positive DSE for ischemia in the absence of ≥ 50% coronary artery lesion in a major artery of the corresponding coronary territory on subsequent angiography.

Patients were divided into 2 groups regarding the presence or the absence (15,5% true positives, 79,7% true negatives, 0,3% false negatives) of a FP result on DSE and a comparative analysis was performed in order to characterize the groups and identify potencial predictors of FP results. (Figure I). Patients were followed for 2 years to assess acute myocardial infarction, hospitalization for acute heart failure and mortality.

Figure I. Study design.



Dobutamine stress echocardiography protocol

The routine institution protocol was applied to all patients and included a staged dobutamine infusion starting with a 5 mcg/kg/min dose that was increased at three-minute intervals to 10, 20, 30, and 40 ug/kg/min, followed by a final 0,5 mg atropine bolus if the heart rate was < 85% of the age predicted maximum value. Heart rate and electrocardiogram readings were continuously monitored. Blood pressure was measured at rest and at the end of each stage. Echocardiographic images were acquired in the left lateral decubitus position using the apical (two- and four-chambers) and parasternal (short- and long-axis) views of the heart, in a Vivid E9 ultrasound machine, GE Healthcare. Echocardiographic contrast was used to augment endocardial definition when segments were not adequately visualized at rest. The test was considered diagnostic if at least 85% of age predicted maximal heart rate was achieved. A hypertensive response to stress was defined as peak systolic blood pressure ≥ 210mmHg in men and ≥ 190mmHg in women, as previously described.[6] Dobutamine intravenous infusion was terminated if any of the following occurred: obvious echocardiographic positivity; age-predicted maximum heart rate reached; severe hypertension; symptomatic reduction in systolic blood pressure ≥40 mmHg from baseline; sustained supraventricular or ventricular arrhythmias or intolerable side effects. Imaging obtained at resting and stress phase were compared for interpretation of left ventricular size, shape, and function. An expert visual analysis in a standard 16 left ventricle segmentation model was made by two operators to assess left ventricle wall motion abnormalities. Ischemia was defined as the development of hypokinesia, akinesia or dyskinesia during stress of a segment that at rest was normokinetic. The DSE was considered positive for ischemia when ≥ 3 of the 16 segments developed ischemia during stress. Several parameters, including indications for performing DSE, peak heart rate, mean blood pressure value at rest and at peak stage,

presence of chest pain, WMSI, electrocardiographic changes at peak stage and presence of arrhythmias (supraventricular and ventricular), were recorded.

Statistical analysis

Continuous variables were described with measures of central tendency and dispersion (mean and standard deviation or median and interquartile range). Categorical variables were presented as frequencies and percentages. Continuous variables were evaluated by Independent-samples t Test or Mann–Whitney U test, and categorical variables compared with chi-square test. Univariate and multivariate logistic regression analyses were used to identify parameters associated with FP results. A p value < 0.05 was considered statistically significant. All analyses were performed using SPSS Statistics Software for Windows version 23.0 (IBM Corporation).

Results

Study Population

Over a one-year period, 355 consecutive patients at our center underwent DSE to assess for ischemia. The patient characteristics and echocardiographic data are summarized in Table I. Their mean age was 70,3 ± 0,57 years, 134 (37,7%) were women and their mean body surface area (ASC) was 1,85 ± 0,01 cm^2. Regarding cardiovascular risk factors, 77,5% had arterial hypertension, 60,8% dyslipidemia, 34,2% diabetes mellitus, 29,3% were current or former smoker and 22,8% had obesity. In what concerns to comorbidities, 34,6% had chronic kidney disease (stage 3-5), 29,3% had coronary artery disease, 20,3% had previous history of atrial fibrillation/flutter, 11,8% had thyroid dysfunction (mostly hypothyroidism – 9%), 8,8% previous history of stroke or transient ischemic attack and 7,3% had chronic obstructive pulmonary disease. At the time DSE was performed, 64,2% of patients were under medication with beta blockers, 13,2% had complete left bundle branch block and the mean hemoglobin, hematocrit and creatinine values were 13,5 ± 0,09 mg/dL, 40,9 ± 0,27% and 1,07 ± 0,03 mg/dL, respectively. Regarding rest echocardiographic variables, the mean of interventricular septum diastolic thickness and left ventricle diastolic diameter base were 12,1 ± 0,13 mm and 45 ± 0,8 mm, respectively, 43,1% had baseline wall motion abnormalities with a wall motion score index of 1,22 ± 0,31. The mean of left ventricular ejection fraction (LVEF) was 56,5 ± 1,2% with 25,6% had LVEF $< 50\%$. Common clinical indications for DSE included: evaluation of symptoms of chest pain (180 patients, 50,7%) and ischemia in patients with previously known coronary artery disease (76 patients, 21,4%). The mean blood pressure value at rest and at peak stage were 83,6 ± 1,7 mmHg and 104,4 ± 2,4 mmHg, respectively, and 8,5% had hypertensive response. Fifty-five patients (15,5%) had chest pain and 84 patients (23,7%) had electrocardiographic changes during DSE. Eighty (22,5%) patients had a poor image quality and received echocardiographic contrast. (Table I)

Table I. Descriptive statistics of demographic, risk factor and stress test variables of the study population.

Characteristic		**N = 355**
Age (years)		70,3 ± 0,57
Female		134 (37,7%)
ASC (cm^2)		1,85 ± 0,01
Cardiovascular risk factors		
	Hypertension	275 (77,5%)
	Dyslipidemia	216 (60,8%)
	Diabetes mellitus	121 (34,2%)
	Current or former smoker	104 (29,3%)
	Obesity	81 (22,8%)
Other medical history		
	Chronic kidney disease	121 (34,6%)
	Coronary artery disease	104 (29,3%)
	Atrial fibrillation/flutter	72 (20,3%)
	Thyroid dysfunction	42 (11,8%)
	Cerebrovascular disease	31 (8,8%)
	Chronic obstructive pulmonary disease	26 (7,3%)
Medical therapy		
	β-blocker	228 (64,2%)
Laboratory parameters		
	Hemoglobin (mg/dL)	13,5 ± 0,09
	Hematocrit (%)	40,9 ± 0,27
	Creatinine (mg/dL)	1,07±0,03
Baseline electrocardiogram		
	Complete left bundle branch block	47 (13,2%)
Baseline echocardiogram		
	Interventricular septum diastolic thickness (mm)	12,1 ± 0,13
	Left ventricle diastolic diameter base (mm)	45 ± 0.8
	Baseline wall motion abnormalities	153 (43,1%)
	WMSI	1,22 ± 0,31
	LVEF (%)	56,5 ± 1,2
	LVEF < 50%	91 (25,6%)
Indications for performing DSE		
	Chest pain	180 (50,7%)
	Known coronary artery disease	76 (21,4%)
	Heart failure study	47 (13,2%)
	Positive stress test	20 (5,6%)
	Ventricular dysrhythmia	13 (3,7%)
	Complete left bundle branch block	12 (3,4%)
Variables during DSE		
	Poor image quality	80 (22,5%)
	Mean blood pressure value at rest (mmHg)	83,6 ± 1,7
	Mean blood pressure value at peak stage (mmHg)	104,4 ± 2,4
	Hypertensive response	30 (8,5%)
	Mean peak heart rate(beats/min)	141 ± 0,9
	Chest pain	55 (15,5%)
	Electrocardiographic changes	84 (23,7%)
	Arrhythmias	235 (66,4%)
	WMSI	1,2 ± 0,3

Data are shown as N (%) except where otherwise noted. ASC - mean body surface area; DSE - dobutamine stress echocardiography; LVEF - left ventricular ejection fraction; WMSI - wall motion score index

False positives

The FP rate was 4,5% (16 patients). Their mean age was 65,1 ± 2,4 years, 25% were women and their mean body surface area was 28,7 ± 2,7 cm^2. Most of patients had arterial hypertension (93,8%) and dyslipidemia (68,8%), 37,5% had diabetes mellitus and 6,25% were current smoker. Regarding comorbidities, 37,5% had chronic kidney disease (stage 3-5), 18,8% coronary artery disease, 18,8% atrial fibrillation/flutter and 12,5% chronic obstructive pulmonary disease. Most patients (56,3%) were medicated with betablockers during study period, 75% had baseline wall motion abnormalities in transthoracic echocardiogram and 6,3% had complete left bundle branch block. Among patients with a positive stress test, the most common reasons for the test were similarly to study population: chest pain (11 patients, 68,7%) and evaluation of ischemia in patients with previously known coronary artery disease (2 patients, 12,5%). Their mean blood pressure value was 99,3 ± 5,4 mmHg at rest and 140,3 ± 5,6 mmHg at peak stage; 37,5% had hypertensive response. (Table II)

Table II. Demographic, risk factor and stress test variables associated with false-positive stress echocardiograms on univariate analysis.

	False positive (n=16; 4,5%)	No false positive (n=339; 95,5%)	p value
Women (%)	25	38,3	0,31
Age (years)	65,1 ± 2,4	70,5 ± 0,6	0,045
Body mass index (Kg/m²)	28,7± 2,7	29,1 ± 0,4	0,89
Diabetes mellitus (%)	37,5	33,9	0,79
Dyslipidemia (%)	68,8	60,5	0,61
Hypertension (%)	93,8	76,7	0,09
Smoking (%)	6,3	11,5	0,66
Chronic kidney disease (%)	37,5	33,9	0,42
COPD (%)	12,5	7,1	0,33
Atrial fibrillation/flutter (%)	18,8	20,4	0,59
Coronary artery disease (%)	18,8	29,8	0,26
Beta blocker (%)	56,3	64,6	0,33
Hemoglobin (mg/dL)	13,7 ± 0,3	13,5 ± 0,2	0,19
Hematocrit (%)	41,3 ± 0,9	40,9 ± 0,6	0,17
Creatinine (mg/dL)	1,0 ± 0,04	1,1 ± 0,05	0,91
Complete LBBB (%)	6,3	13,6	0,35
ISDT (mm)	12,5 ± 0,7	11,8 ± 0,3	0,41
LV diastolic diameter base (mm)	46 ± 0,5	46 ± 0,7	0.14
Mean resting LVEF (%)	53,6 ± 3,2	52,7 ± 1,8	0,41
Baseline wall motion abnormalities (%)	75,0	41,6	0,009
Rest WMSI	1,1 ± 0,1	1,2 ± 0,2	< 0,001
Stress WMSI	1,2 ± 0,2	1,3 ± 0,3	< 0,001
BP mean values at rest (mmHg)	99,3 ± 5,4	82,0 ± 1,3	0,004
BP mean values at peak stage (mmHg)	140,3 ± 5,6	102,8 ± 2,3	< 0,001
Peak heart rate (beats/min)	144,1 ± 5,0	138,8 ± 2,8	0,42
Hypertensive response (%)	37,5	7,1	<0,001
Electrocardiographic changes (%)	1,1	5,9	<0,001
Presence of chest pain at stress (%)	31,3	26	0,11
Good technical quality (%)	81,3	80	0,47

CAD – coronary artery disease; COPD - chronic obstructive pulmonary disease; ISDT - interventricular septum diastolic thickness; LV – left ventricular; LVEF - left ventricular ejection fraction; LBBB – left bundle branch block; WMSI - wall motion score index.

No false positives

There were 339 (95,5%) patients without a false positive result: 15,5% were true positives, 79,7% were true negatives and 0,3% were false negatives. 38,3% of these patients, were female, they had a mean age of 70,5 ± 0,6 years and a mean body surface area of 29,1 ± 0,4 cm^2. Cardiovascular risk factors were prevalent: arterial hypertension (76,7%), dyslipidemia (60,5%), diabetes mellitus (33,9%) and smoking (11,5%). Chronic kidney disease (stage 3-5) was present in 33,9%, 29,8% of patients had coronary artery disease, 20,4% atrial fibrillation/flutter and 7,1% chronic obstructive pulmonary disease. Most patients (64,6%) were medicated with betablockers during the study period, 13,6% had complete left bundle branch block and 41,6% showed baseline wall motion abnormalities in transthoracic echocardiogram. Their mean blood pressure value was 82,0 ± 1,3 mmHg at rest and 102,8 ± 2,3 mmHg at peak stage, and 7,1% had hypertensive response. (Table II)

False positives vs No false positives

In the comparative analysis with patients without false positive results, the patients with a false positive DSE were younger (65,1 ± 2,4 vs 70,5 ± 0,6 years; p=0,045). During DSE, higher mean values of blood pressure at rest (99,3 ± 5,4 vs 82,0 ± 1,3 mmHg; p=0,004) and at peak stage (140,3 ± 5,6 vs 102,8 ± 2,3 mmHg; p < 0,001) and hypertensive response (37,5% vs 7,1%; p < 0,001), were more commonly associated with a FP result. There were no significant differences between the two groups regarding previous coronary artery disease, medication or complete left bundle branch block. Positive results on stress electrocardiogram were present in a minority of patients. Negative results on stress electrocardiogram were independently associated with angiographically mild (<50%) coronary artery disease and/or normal coronary arteries. Regarding echocardiographic variables, stress echocardiograms with higher baseline wall motion abnormalities (75,0% vs 41,6%; p=0,009), lower rest WMSI (p = 0.004) and lower stress WMSI (p < 0.001) were also more likely to be FP. There were no significant differences between the two groups regarding left ventricular ejection fraction at rest and at peak heart rate. (Table II) By multivariate analysis, only mean blood pressure values at rest (OR 0,01; 95%CI 0,005-0,02; p=0,003) and at peak stage (OR 0,02; 95%CI 0,000-0,004; p=0,003) were independent predictors of FP. (Table III)

Table III. Demographic, risk factor and stress test variables associated with false-positive stress echocardiograms on multivariate analysis.

Variable	False-positive stress echocardiogram	
	OR (95% CI)	**p-value**
Age (years)	0,99 (0,96 - 1,00)	0,270
Mean blood pressure values at rest	0,01 (0,005 - 0,02)	0,003
Mean blood pressure value at peak stage	0,02 (0,000 - 0,004)	0,003
Hypertensive response (%)	0,87 (0,51 – 1,27)	0,346
Electrocardiographic changes (%)	0,66 (0,31 – 1,37)	0,264
Baseline wall motion abnormalities (%)	0,84 (0,48 – 1,19)	0,235
Rest WMSI	0,94 (0,67 – 1,33)	0,622
Stress WMSI	0,81 (0,48 – 1,33)	0,582

WMSI - wall motion score index.

During an average follow-up period of two years, a total of 22 patients (6,2%) died, among whom 1 had a FP result test (6,3%) and 21 had not FP stress test (6,2%) (p=0,65). Rergardly to the other outcomes evaluated, 8 patients had acute myocardial infarction (2,3%): 2 patients (12,5%) from the group of FP results and 6 patients (1,8%) from the group without FP results (p= 0,046); and 40 (11,3%) had hospitalizations for acute heart failure: 39 patients (11,5%) without false-positive results and 1 patient (6,3%) with false positives (p=0,44) (Table IV).

Table IV. Prognostic value of false positive results for *outcomes* during follow-up.

	False positive (n=16; 4,5%)	No false positive (n=339; 95,5%)	p value
Acute myocardial infarction (%)	12,5	1,8	0,046
Hospitalization for acute heart failure (%)	6,3	11,5	0,44
Mortality (%)	6,3	6,2	0,65

After adjustment for age, sex and comorbidities, there were no diferences between the groups regarding hospitalization for acute heart failure (p=0,45) and mortality (p=0,77), but the group with false positive results mantained a higher rate of acute myocardial infarction (OR 0,21; 95%CI 0,065-0,354; p=0,005). (Table V)

Table V. Prognostic value of false positive results for *outcomes* during follow-up after adjustment.

	OR (95% CI)	**p-value**
Acute myocardial infarction (%)	0,21 (0,065 – 0,354)	0,005
Hospitalization for acute heart failure (%)	1,04 (0,55 – 1,94)	0,45
Mortality (%)	1,11 (0,99 - 1,15)	0,77

Discussion

Current practice guidelines recommend the performance of stress echocardiography in patients with high pre-test probability in which the revascularization is likely. DSE is an important tool for evaluating patients with suspected coronary arterial disease, however, FP results often lead to unnecessary invasive procedures. In our study 4,5% (16 patients) had a FP result, which was lower than the described in other studies. Patel et al. reported that only 41% patients with a positive non-invasive test having obstructive coronary artery disease on elective cardiac catheterization.[6] Similar results were previously reported by Rachwan et al. with 162 patients (53%) had a FP result among the 305 patients[2]. From et al. showed that 9,5% of 1477 patients with abnormal results on stress echocardiography had normal coronary arteries at the time of coronary arteriography and 23% of patients had mild, nonobstructive coronary artery disease (<50% stenoses).[3] Batch et al. reported 11,4% of FP results.[5]

In our study, the young age, baseline wall motion abnormalities, and lower rest and stress WMSI, were significantly associated with FP results on univariate analysis but lost significance after adjusting for potential confounders. However, higher mean blood pressure values at rest and at peak were independent predictor of FP results. Several studies identified as possible predictors of FP in DSE the female gender[2,4,5], the absence of diabetes mellitus[2,4], a hypertensive response to exercise[4] and wall motion abnormalities of the middle and apical segments of the left ventricle[4]. Rachwan et al. showed that in a group of 5100 patients the female gender (56% vs 31%, p < 0,001), the absence of diabetes (59% vs 40%, p = 0,001) and the absence of a previous history of coronary artery disease (69% vs 35%, p < 0,001) were independently associated with FP results.[2] Similarly, in an analysis of 342 stress echocardiograms, Bach et al. reported that more than 70% of the patients with FP results were women, with an incidence of FP studies of 20,9% (28 of 134) for women and 5,3% (11 of 208) for men[5]. In line with these finding, Qamruddin et al. reported that nondiabetic patients and younger females were most likely to have a FP in DSE in a group of 1477 patients, and the hypertensive response to exercise and alterations in segmental contractility of the middle and apical segments of the left ventricle were also predictors of FP results[4].

In our study, a false positive result on dobutamine stress echo was associated with a higher rate of acute myocardial infarction. Recent studies suggested that irrespective of angiographic findings the patients with abnormal DSE results are at higher risk for major cardiovascular events compared to patients with normal results[3,8,9]. Sicari et al. evaluated the prognostic role of dipyridamole stress echocardiography in patients with angiographically normal coronary arteries over a period of 140 months and found that patients with FP results had a lower survival rate compared to those with negative results (90% vs 76%, p = 0.0018)[10]. There is a physiological

rationale to this effect as we can hypothesize a possible relation with microvascular abnormalities, vasomotor changes, endothelial dysfunction, and/or small vessel coronary disease that can lead to false-positive stress echocardiography and a worst prognosis. This could occur at least in a subset of patients, in this case not truly corresponding to false positive result on DSE but rather to ischemia without obstructive coronary arteries (INOCA). A review of the literature shows that patients with abnormal DSE results are at higher risk for major adverse events compared to patients with normal results, irrespective of angiographic findings.[3,8,9] Gilchrist et al. studied 1299 patients undergoing SE. Authors found 43 of the 83 positive stress tests to be FP and these patients are at increased risk of major cardiac events (namely myocardial infarction, heart failure or death from any cause) compared to those with negative DSE results (20.9% vs. 6.2%, p=0.012), with the average time to an event of 4 years in both groups.[9] This poses diagnostic and management challenges since these patients have been historically treated as if they had no significant coronary artery disease and are usually dismissed from the care of cardiologists.

Our study has several limitations. First, our data were collected and analyzed retrospectively, so some measurements were not available for all patients. Second, image interpretation was performed only by the exam operator and despite the high experience of the operators, it would have been preferable to confirm inter observer agreement. Thirdly, we describe the results of a single center study with a limited number of enrolled patients. A larger sample from other centers would better assess the prognostic value of FP result on stress echocardiography and would validate our results. Finally, our findings show that outcomes are similar after abnormal stress echocardiographic results, regardless of the findings on subsequent angiography, so it would be important to have continued with the study with the performance of other complementary diagnostic tests, to elucidate the underlying causes of false-positive results associated to an intensive risk factor management and routine follow-up.

For these reasons, these findings should be confirmed in further studies, preferably in a randomized trial, with a larger sample and inclusion of other complementary diagnostic tests (namely, invasive functional tests to assess ischemia) in the protocol, to explore the clinical significance of false positive results.

Conclusions

Our study showed that the positive predictive value of stress echocardiography is lower for higher mean blood pressure values during the test. FP results were associated with higher rates of acute myocardial infarction during follow-up comparatively with negative results DSE, which is in line with the finding of other studies and seems to correspond to INOCA with a worse prognosis. Therefore, attention should be given to false-positive stress echocardiography results with a more aggressive risk factor control and a careful clinical follow-up of these patients. Further investigation, with functional ischemia tests, is needed to better characterize this population and unravel the pathophysiology of a worse prognosis.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

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