Stress Echocardiography in a Caribbean Population: Predictors and Performance

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Received Date: 14 September, 2018; Accepted Date: 20 September, 2018; Published Date: 01 October, 2018

Abstract

Background: Stress echocardiography is a well-established procedure for diagnosis of coronary artery disease. Its utility in the Caribbean population is still being explored. The aim of our study was to explore incidence of abnormal stress echocardiography and ascertain ischemia predictors in consecutive patient’s cohort referred to cardiology clinic in Jamaica.

Methods: Retrospective analysis of the data of 481 patients referred to Heart Institute of the Caribbean, Kingston, Jamaica for stress echocardiography from 2012 to 2016. Independent predictors of ischemia on stress echocardiography was identified by using multivariate logistic regression analysis.

Results: The cohort average age was 61 years, 58.4% were females. 32.6% of patients underwent exercise Stress echocardiography, 67.4% of patients underwent dobutamine Stress echocardiography. 18.4% of subjects had new wall motion abnormalities suggestive of ischemia. In multivariate logistic regression model, age (OR 1.028; p=0.012) and male gender (OR, 2.35; P = 0.005) were shown to be significant independent predictors of a positive stress echo result in this population.

Conclusions: Stress echocardiography is outstanding noninvasive safe tool for detection of ischemia. Incidence of ischemia among unselected Jamaican patient population referred for stress echocardiography at Heart Institute of the Caribbean was about 18.4% and coronary artery disease is more likely to be present in men and the elderly.

Keywords: Caribbean Population; Coronary Artery Disease; Stress Echocardiography

Abbreviations

BP : Blood Pressure
BMI : Body Mass Index
CAD : Coronary Artery Disease
DM : Diabetes Mellitus
ECG : Electrocardiogram
HIC : Heart Institute of the Caribbean
LV : Left Ventricle
LVEF : Left Ventricular Ejection Fraction
MACE : Major Adverse Cardiac Events
RPP : Rate Pressure Product
SE : Stress Echocardiography
THR : Target Heart Rate
WMA : Wall Motion Abnormalities
Introduction

Stress Echocardiography (SE) is a well-established procedure for the diagnosis of Coronary Artery Disease (CAD) as the imaging modality can reveal new or worsening regional Wall Motion Abnormalities (WMA) in ischemic coronary artery territory [1]. Combination of echocardiography imaging with a physical or pharmacological stress enhances accuracy of stress Electrocardiogram (ECG) for apperception of ischemia [2].

SE provides comparable efficiency to myocardial stress perfusion imaging in detection of CAD, but at considerably improved economic cost and without radiation hazards on environment, operator and the patient [3].

SE reports variable sensitivity (54% to 96%) and specificity (62% to 93%). Several factors are thought to be the cause of such differences in reported accuracy such as patient clinical demographics, coronary angiography referral tendency, and other procedural factors [4].

Different ethnic population demonstrated variable proportion of coronary disease [5-7]. Atherosclerosis Risk in Communities (ARIC) Project sponsored by the National Heart, Lung, and Blood Institute, reported similar risk factors for atherosclerosis among African-Americans and Caucasians, however significant clinical racial variation exists [8]. CAD presentation is comparable among both African Americans and whites, nevertheless greater risk for sudden cardiac death, non-Q-wave myocardial infarction and presentation with unstable angina in African Americans than whites. African Americans have less obstructive CAD on angiograms, but may have a similar or greater total burden of coronary atherosclerosis. This could be due to genetic heterogeneity of coronary syndromes, and the high prevalence and severity of type 2 diabetes and hypertension in African Americans. Identification of high-risk individuals for vigorous risk factor modification is the key for successful risk reduction [9].

While SE is commonly used for cardiac diagnostic work up of patients in the Caribbean. There is no prior report in the literature from the Caribbean that explores the outcome of SE in the Caribbean population. The aim of this study is to recognize characteristics of patients undergoing SE in an outpatient cardiology practice in Jamaica and identify predictors associated with a positive SE report.

Methods

Retrospective analysis of patients referred to Heart Institute of the Caribbean (HIC) for SE from January 2012 to October 2016. Patient’s data were collected from medical records, SE exam sheets and reports. All patients underwent exercise SE or dobutamine SE were included in our study. Clinical characteristics including a history of hypertension, diabetes, hypercholesterolemia, cigarette smoking clinical presentation and prior history of CAD were recorded for all patients.

Exercise Stress Echocardiography

Patients without significant functional limitations underwent exercise stress testing. standard Bruce protocol was used [10]. Exercise stress test was terminated if the patient was unable to continue due to fatigability, patient’s request or if the patient developed severe angina pain, serious arrhythmia or hemodynamic instability. Echocardiographic images post-exercise was obtained within 30 to 60 seconds after termination of exercise.

Dobutamine Stress Echocardiography

Patients with functional limitations who were unable to undergo treadmill exercise test or were unable to achieve target heart rate (defined as 85% of the maximal age-predicted heart rate) despite maximal effort underwent Dobutamine SE. Incremental Dobutamine infusion started with a dose of 10 mg/kg/min and increased by 10 mg/kg every 3 min to a maximum of 40 mg/kg/min or until target heart rate achieved. Atropine was administered intravenously in 0.25- mg increments every 3 min to a maximum of 1 mg if target heart rate was not achieved at the maximum dobutamine dose [11]. Dobutamine infusion was terminated if target heart rate was achieved or if target heart rate was not achieved in spite of greatest doses of medications were given, evolving of significant new WMAs, serious adverse effects related to medications and patient’s request to discontinue test. Patient was monitored although the test with 12-lead ECG and Blood Pressure (BP) readings recorded at rest, at each level of stress, and during the recovery phase.

Echocardiographic Image Acquisition

All studies were performed by Technicians who are formally trained and certified in the performance of SE and had at least 3 or more years of experience performing these studies. Echocardiographic images were acquired using General Electric (GE) Vivid 5, GE Vivid 7 and GE Vivid I echo machines with harmonic imaging and phased array probes.

Several Echocardiographic views were obtained: parasternal long-axis, parasternal short-axis, apical four chamber and apical two-chamber. Echocardiographic images were acquired at each stage; rest images, low-dose dobutamine images, peak images with high dobutamine dose or immediately after exercise.

Echocardiographic Measurements and Image Analysis

Study were interpreted by experienced board-certified cardiologists with level 2 or level 3 training in echocardiography, according to HIC protocol. Study analysis according to American Society of Echocardiography (ASE) guidelines. Left ventricle (LV) was divided into 16 segments, and a score was assigned to
each segment: 1 = normal, 2 = mild to moderate hypokinesis, 3 = severe hypokinesis, 4 = akinesis, or 5 = dyskinesis [12,13].

Normal wall motion response was defined as increase in wall thickening and excursion both at rest and stress. Abnormal response was defined as (1) LV wall segment that did not increase in thickening and excursion during stress, (2) a deterioration in LV segment wall thickening and excursion during stress (increase in wall motion score of >1 grade), and (3) a biphasic response with dobutamine stress [14].

Statistical Analysis

Statistical analysis was performed with SPSS Version 20 (IBM Corporation, NY, USA) for Windows. Continuous data were explored for normality by checking the data distribution, calculating the mean and median values and using Kolmogorov-Smirnov and Shapiro-Wilk tests. Data showed normal distribution. Continuous Data were presented by mean and Standard Deviation (SD) values. Categorical data presented as frequency and percentage. Chi square test was used to assess associations between categorical data. Logistic regression models were used to recognize independent predictors of abnormal SE. age, gender, BMI, diabetes mellitus, chest pain, HTN, dysipdemia, dyspnea, and abnormal ECG. BMI, diabetes mellitus, chest pain was included as predictors and abnormal SE result was included as an outcome variable in the initial binary logistic regression model. Forward stepwise selection strategy was used to generate final multivariate logistic regression model. The significance level was set at p ≤ 0.05.

Institutional review board approved by the study.

Results

A total of 481 patient records were reviewed. Mean age of the cohort was 61 years, 58.4% were females. Only 2% of patients had previously diagnosed CAD. Cardiovascular risk factors included; hypertension (42.9%), diabetes mellitus (18.1%), hyperlipidemia (10.4%), smoking (0.4) and obesity (body mass index [BMI] > 30 kg/m2) (45.9%). Clinical presentation; chest pain (35.4%), dyspnea (16.2%), abnormal resting ECG (6.9%). Resting left ventricular ejection fraction (LVEF) was normal in 92.2% of patients, mildly decreased in 4.5% of patients, moderately decreased in 2.1% of patients and severely decreased in 1.2% of patients. 35.7% of patients underwent exercise stress; rest of the patients (64.3%) underwent dobutamine stress. Summary of the patient characteristics is presented in Table 1.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>200/481</td>
<td>41.6%</td>
</tr>
<tr>
<td>female</td>
<td>281/481</td>
<td>58.4%</td>
</tr>
<tr>
<td><strong>HTN</strong></td>
<td>206/480</td>
<td>42.9%</td>
</tr>
<tr>
<td><strong>DM</strong></td>
<td>87/480</td>
<td>18.1%</td>
</tr>
<tr>
<td><strong>Dyslipidemia</strong></td>
<td>50/480</td>
<td>10.4%</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>1/224</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>Obesity (BMI &gt; 30kg/m²)</strong></td>
<td>166/307</td>
<td>54.1%</td>
</tr>
<tr>
<td><strong>Prior history of CAD</strong></td>
<td>6/312</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Chest pain</strong></td>
<td>170/480</td>
<td>35.4%</td>
</tr>
<tr>
<td><strong>Dyspnea</strong></td>
<td>78/480</td>
<td>16.2%</td>
</tr>
<tr>
<td><strong>Abnormal resting ECG</strong></td>
<td>33/480</td>
<td>6.9%</td>
</tr>
<tr>
<td><strong>Resting LVEF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>431/467</td>
<td>92.2%</td>
</tr>
<tr>
<td>Mildly decreased</td>
<td>20/467</td>
<td>4.5%</td>
</tr>
<tr>
<td>Moderately decreased</td>
<td>9/467</td>
<td>2.1%</td>
</tr>
<tr>
<td>Severely decreased</td>
<td>5/467</td>
<td>1.2%</td>
</tr>
<tr>
<td><strong>Type of stress Test</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise SE</td>
<td>140/392</td>
<td>35.7%</td>
</tr>
<tr>
<td>Dobutamine SE</td>
<td>252/392</td>
<td>64.3%</td>
</tr>
</tbody>
</table>

HTN; Hypertension, DM; diabetes mellitus, BMI; Body Mass Index, CAD; Coronary Artery Disease, ECG: Electrocardiogram, LVEF; Left Ventricular Ejection Fraction, SE; Stress Echo.

Table 1: Patient categorical variables (presented as percentages).
Recorded dobutamine doses showed that the majority of patient underwent dobutamine SE received a max dose of 40 mg/kg/min, 196/232 patients (84.5%) (Table 2). Atropine (0.25-1 mg) was given to 22% of patients who had the dobutamine SE. Recorded data showed a low incidence of chest pain with both types of stress modalities with total incidence of 2.8%, positive ECG changes was recorded in 6.1% of patients, and were more likely to be present with a positive SE (31%). Blood pressure drop was recorded in 13.8% of patients, and was more common in patients undergoing the dobutamine SE ($p < 0.001$) (Table 3). No major adverse cardiac events (MACE) was recorded with both types of stress modalities.

<table>
<thead>
<tr>
<th>Dobutamine dose used (mg/kg/min)</th>
<th>Number of patients N=232</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>3</td>
<td>1.3%</td>
</tr>
<tr>
<td>20</td>
<td>12</td>
<td>5.2%</td>
</tr>
<tr>
<td>30</td>
<td>21</td>
<td>9%</td>
</tr>
<tr>
<td>40</td>
<td>196</td>
<td>84.5%</td>
</tr>
</tbody>
</table>

Table 2. Different dobutamine doses used.

Majority of patient underwent dobutamine SE received maximum dose of dobutamine.

<table>
<thead>
<tr>
<th>Type of test</th>
<th>Test result</th>
<th>Number of patients (N)</th>
<th>Chest Pain</th>
<th>Positive ECG</th>
<th>Hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>positive</td>
<td>41</td>
<td>4</td>
<td>13</td>
<td>51 ($p &lt; 0.001$)</td>
</tr>
<tr>
<td></td>
<td>negative</td>
<td>211</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>positive</td>
<td>27</td>
<td>0</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>negative</td>
<td>113</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>392</td>
<td>11 (2.8%)</td>
<td>24 (6.1%)</td>
<td>54(13.8%)</td>
</tr>
</tbody>
</table>

Table 3. Prevalence of abnormal findings during Stress Echocardiography.

Chi square test was used to assess associations between chest pain, ischemic ECG changes and hypotension with stress echo results. Abnormal BP response was statistically greater ($p < 0.001$) with dobutamine stress compared to exercise stress.

The average Target Heart Rate (THR) achieved 99% +12 in both exercise and dobutamine stress patients. 67.4% achieved THR, 2.8% of patients developed chest pain, and 6.1% of patients had positive ECG changes. Rate Pressure Product (RPP) was significantly higher in exercise group.

During the stress portion of the test, 89/481 (18.4%) of patients had new WMAs consistent with ischemia: 52/89 (58.4%) with exercise and 37/89 (41.6%) with dobutamine. 9 subjects (1.9%) had test results that were inconclusive (Table 4).

<table>
<thead>
<tr>
<th>B</th>
<th>S.E.</th>
<th>Sig.</th>
<th>Exp (B)</th>
<th>95% C.I. for EXP (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>Male Gender</td>
<td>.977</td>
<td>.318</td>
<td>.002</td>
<td>2.657</td>
</tr>
<tr>
<td>BMI</td>
<td>.031</td>
<td>.022</td>
<td>.171</td>
<td>1.031</td>
</tr>
<tr>
<td>Age</td>
<td>.029</td>
<td>.012</td>
<td>.013</td>
<td>1.030</td>
</tr>
<tr>
<td>Chest pain</td>
<td>-.327</td>
<td>.351</td>
<td>.352</td>
<td>.721</td>
</tr>
</tbody>
</table>

Table 4: Prevalence of abnormal wall motion in study cohort.

The initial logistic regression model showed Age (OR 1.030; $p=0.013$) and Male gender (OR, 2.657; $P = 0.002$) were significant predictors for positive SE test results on the other hand patient’s BMI, history of diabetes mellitus, hypertension, dyslipidemia or presence of chest pain, dyspnea or abnormal ECG did not predict positive results (Table 5).
Age and male genders were the only significant independent predictors for abnormal SE test, and remained significant in the final logistic model. BMI; Body Mass Index, HTN; Hypertension, DM; Diabetes Mellitus, ECG; Electrocardiogram.

In the final logistic regression model age (OR 1.030; p=0.013) and male gender (OR, 2.657; P = 0.002) remained significant independent predictors of a positive SE result in this population.

Chi square test was used to find correlation between test result and LVEF. There was a significant correlation between a positive test result and a decrease in LVEF (p=0.001).

**Discussion**

SE is a well-established technique for diagnosis of CAD. SE provides significant improvements in test accuracy over the exercise stress test [15-17]. Our study showed a significant correlation of age with positive stress test results. This finding is in concordance with multiple previous studies, and probably attributed to the increase of prevalence and severity of CAD with age [18-21]. A similar result was shown by a meta-analysis of 62 studies, including 6881 patients, which analyzed patient characteristics, and assessed their effect on the diagnostic validity of dobutamine SE [4]. Regression model analysis in our study showed that males were likely to have more positive stress echo studies than females. Elhendy et al. 1997 showed similar results, they investigated the impact of gender on reliability of dobutamine SE for detection of CAD in 306 patients with limited exercise endurance and presumed CAD. WMA score index was greater in men than in women at rest (1.59 ± 0.46 vs 1.40 ± 0.46, p <0.005) and at peak stress (1.76 ± 0.53 vs 1.49 ± 0.52, p <0.0005) [22]. Another study of gender dissimilarity for predicting outcome among 581 men and 309 women with verified or presumed CAD. Women had less WMAs at rest and at peak stress, with less prevalence of positive results of dobutamine SE compared to men [23]. PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial indicated that CAD diagnosis, presentation and risk factors is affected by gender, with more positive test results in males 15.1% compared to females 9.7% [24]. Risk of CAD in male are greater in males compared to females with higher likelihood of having positive SE. There is a known protective influence of estrogen from heart disease in premenopausal women [26-28].

No significant correlation was found between different CAD risk factors and the test results. Diabetes mellitus (DM) is one of the dominant risk factors that has dramatically increased over the last few decades not only in modernized countries, [29] but also in developing countries such as African countries due to the change of diet habits with the introduction of high calorie “western-diet”, increased obesity prevalence and the changeover in lifestyle with physical inactivity [30]. The National Cholesterol Education Program (NECP) Adult Treatment Panel (ATP) III guidelines in 2001 recommended that all individuals with DM be considered as CAD risk equivalent [31]. Several studies showed significant correlation of DM and the development of new WMAs on SE [32,33]. The inability of our study to show the correlation of DM and the results of SE could be explained by small study group and referral bias with low presentation of DM in the study population (18%).

Driscoll et al., examined the anticipating value of dobutamine SE among the British-Indian-Asian and Afro-Caribbean population including 621 subjects and using future morbidity and mortality data. A strong correlation between abnormal Dobutamine SE and non-fatal cardiac events and all-cause mortality among these ethnic populations [34]. Khan et al. in Detroit and Sawada et al. in Indianapolis also investigated the predictive utility of dobutamine SE in an African-American population and found that dobutamine SE predicted mortality and major adverse cardiac events in that population, making it a useful tool in coronary disease management [35,36]. Sutter et al., suggested a risk scoring system that can ameliorate prediction of cardiovascular events in African Americans with normal results on stress echocardiography. This will be helpful for the cases of false negative results from SE in this population [37]. Our study on the performance of the stress echocardiogram in the Caribbean population adds to these studies to show that SE can be of utility in coronary disease assessment in the Black population.

Our study has a few limitations which include a relatively small sample size and the lack of cardiac catheterization data in the

| Table 5: Clinical features statistically associated with abnormal wall motion (multivariable analysis; initial logistic regression model). |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| HTN                             | -.034           | .326            | .918            | .967            | .511            | 1.831           |
| DM                              | .167            | .403            | .678            | 1.182           | .537            | 2.602           |
| Cholesterol                     | -.599           | .577            | .299            | .549            | .177            | 1.701           |
| Dyspnea                         | .472            | .425            | .266            | 1.603           | .698            | 3.685           |
| Abnormal ECG                    | .311            | .544            | .567            | 1.365           | .470            | 3.961           |

analysis to discuss the accuracy, sensitivity and specificity of the stress echocardiogram in our center. Interpretation of wall motion abnormality is also subjective and depends on the experience of the operator. However, previous data from our echocardiography lab have shown significant correlation of stress echocardiography with cardiovascular outcomes.

**Conclusion**

SE is an important noninvasive safe tool for detection of ischemia, the incidence of ischemia among unselected Jamaican patient population referred for SE at HIC was about 20%. Ischemia is more likely to be present in men and elderly in our population.

**References**


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