**Artigo Original**

**Ecocardiografia com Contraste Miocárdico e Cintilografia de Perfusão Miocárdica Sincronizada ao Eletrocardiograma na Avaliação de Pacientes com Dor Torácica.**

**Contrast Echocardiography and Gated Perfusion Imaging in the Evaluation of Patients with Chest Pain**

Silvia Moreira Ayub Ferreira¹, José Soares Junior², Jeane Mike Tsutsui³, Marcia Azevedo Caldas⁴, João Cesar Nunes Sbano⁵, Protássio Lemos da Luz⁶

**RESUMO**

**Introdução:** A avaliação de pacientes com dor torácica é muitas vezes problemática. O desafio em diagnosticar corretamente a etiologia da dor torácica é dificultado pela baixa sensibilidade dos métodos diagnósticos disponíveis. Neste estudo, avaliou-se a utilidade diagnóstica da ecocardiografia com contraste miocárdico (MCE) e da cintilografia de perfusão miocárdica sincronizada ao eletrocardiograma (G-SPECT) para detecção de isquemia miocárdica. **Métodos e Resultados:** Dezoito pacientes atendidos no pronto socorro, para avaliação da dor torácica sugestiva de angina, foram submetidos à MCE e G-SPECT. Para ambos os métodos, a perfusão miocárdica e a mobilidade foram avaliadas nos mesmos sete segmentos do ventrículo esquerdo. As imagens foram classificadas como positivas ou negativas para isquemia. Um segmento era considerado positivo na presença de um defeito da perfusão e uma anomalia do movimento da parede. A cinecorticortografia foi realizada se MCE ou G-SPECT foram classificados como positivos para isquemia. Se ambos os exames foram negativos, o paciente foi submetido ao G-SPECT de estresse no dia seguinte. Sensibilidade e especificidade para detecção de isquemia miocárdica foram, respectivamente: A) G-SPECT: 1. avaliação de perfusão: 100% e 75%; 2. avaliação de contração: 66% e 91.6%; 3. associação perfusão+contração: 66% e 91.6%. B) MCE: 1. avaliação de perfusão: 20% e 76%; 2. avaliação de contração: 33,3% e 83,3%; 3. associação perfusão+contração: 0% e 84,6%. **Conclusões:** G-SPECT mostrou-se um bom exame para a detecção de isquemia miocárdica em pacientes de baixo risco. O MCE, na metodologia utilizada, não mostrou capacidade diagnóstica satisfatória.

**Descritores:** Dor no Peito, Isquemia Miocárdica, Tomografia Computadorizada de Emissão de Fóton Único, Ecocardiografia.

**SUMMARY**

**Background:** The evaluation of patients presenting to the emergency department with chest pain is often problematic. The challenge of correctly diagnosing the etiology of chest pain is hindered by the low sensitivity of available clinical tools. In this study, we evaluated the potential diagnostic usefulness of gated¹⁹⁹mTc-sestamibi single-photon emission computed tomography (G-SPECT) and myocardial contrast echocardiography (MCE) for detection of myocardial ischemia. **Methods and results:** Eighteen patients were seen in the emergency room for evaluation of angina-like chest pain and were submitted to MCE and G-SPECT. For both methods, myocardial perfusion and wall motion were assessed in the same seven segments of left ventricle. Images were classified as positive or negative for ischemia. A positive segment required a perfusion defect or a wall motion abnormality. Coronary angiography was performed if MCE or G-SPECT images were classified as positive for ischemia. If both exams were negative, the patient was submitted to SPECT stress on the next day. Sensitivity and specificity for detection of myocardial ischemia were: A) G-SPECT: 1. perfusion scores: 100 and 75%; 2. wall motion scores: 66 and 91.6%; 3. association perfusion+wall motion: 66 and 91.6%. B) MCE: 1. perfusion scores: 20 and 76%; 2. wall motion scores: 33.3 and 83.3%; 3. association perfusion+wall motion: 0 and 84.6%. **Conclusions:** G-SPECT in low risk patients can successfully identify acute cardiac event. The MCE did not show enough accuracy to detect myocardial ischemia.

**Descriptors:** Chest Pain; Myocardial Ischemia; Tomography, Emission-Computed, Single Photon; Chest Pain; Echocardiography.
Introduction

The evaluation of patients presenting to the emergency department with chest pain is often problematic. Many of these patients are admitted, although most are latter determined to have non-ischemic causes of their symptoms. In the other hand, 2-8% of patients with acute myocardial infarction who present to the emergency department are sent home, with a significant increase in morbidity and mortality. The challenge of correctly diagnosing the etiology of chest pain is hindered by the low sensitivity of available clinical tools. The sensitivity of initial biochemical markers (creatine kinase-MB and troponin T) and electrocardiogram (ECG) changes in patients with suspected acute ischemia obtained at arrival to the emergency department is low (about 20% and 50%, respectively).

Many studies have used technetium-99m sestamibi single-photon emission tomography (SPECT) for the evaluation of chest pain, which have evolved into a powerful tool with a negative predictive value for acute ischemic syndromes of 95-100%.

Recent advances have enabled the detection of myocardial perfusion with myocardial contrast echocardiography (MCE). For the evaluation of coronary artery disease, the concordance between MCE and SPECT at rest and stress was 90% (κ=0.77). Furthermore, MCE has been used in patients with chest pain and those with abnormal regional function were 6.1 times as likely to have an early coronary event compared with those with normal regional function. Another study that compared SPECT and MCE to evaluation of chest pain showed a concordance between both methods of 77%. It must be emphasized that both studies included patients with previous myocardial infarction or abnormal electrocardiogram.

In this study, we evaluated the potential diagnostic usefulness of myocardial contrast echocardiography in comparison with gated single-photon emission tomography (G-SPECT) to the evaluation of chest pain in patients without history of myocardial infarction.

Methods

Patients population and study protocol

The study group comprised 18 patients seen in the emergency room for evaluation of angina-like chest pain. The inclusion criteria were chest pain lasting ≥ 30 minutes and occurring within 6 hours of emergency room presentation and a normal or nondiagnostic 12-lead ECG. Exclusion criteria were historical or ECG evidence of previous myocardial infarction, ECG evidence of ischemia (ST segment elevation, ≥ 1 mm ST segment depression or new T wave inversion), pregnancy and lactation.

When inclusion and exclusion criteria were met and after giving informed consent, patients were submitted to MCE and G-SPECT. MCE was undergone first but 99mTc-sestamibi was injected at the same time of the beginning of infusion of microbubbles. G-SPECT was performed after the end of MCE. Serial enzyme determinations were performed every 6 hours for ≥ 12 h and 12 lead ECG were obtained at admission and 24 h later. Coronary angiography was performed if MCE or G-SPECT images were classified as positive for ischemia. If both exams were negative, the patient was submitted to SPECT stress using either the Bruce protocol or pharmacologic stress with dipyridamole on the next day.

The study protocol was approved by institutional ethics committee and all patients provided written informed consent.

Myocardial contrast echocardiography

The contrast agent used for this study was a perfluorocarbon-filled microbubble (PESDA). The images were obtained using a digital ultrasound system (HDI-3000-ATL). A broadband transducer that transmits at a mean frequency of 2.0 MHz and receives at a mean frequency of 4.0 MHz (harmonic) was used for imaging. A dynamic range of 50 dB was used. Images were stored on videotape.

Fundamental cross sectional echocardiography images from the three apical views were recorded before any contrast was injected for assessment of regional wall motion. After acquisition of funda-
mental images, the imaging mode was switched from fundamental to harmonic.

The contrast PESDA was used at dose of 0.1/ 
ml/kg diluted in 80 ml of saline solution and infused at a rate of 2 to 5 ml/min. Image was acquired in the three apical views. As soon as the contrast agent was injected, imaging was switched from continuing to intermittent. In the intermittent mode, ultrasound is transmitted once every one or more cardiac cycle. By gating to the peak of the T wave on the ECG, images were acquired at the end of systole.

**Gated single-photon emission tomography**

Patients were injected with ~ 25–30 mCi of 99mTc sestamibi at the same moment that started microbubbles infusion. G-SPECT was performed using a dual-headed gamma camera system. High-resolution, low energy, parallel-hole collimators were used to record data onto a 64x64 image matrix. Gated acquisition using eight time frames per cardiac cycle was done. All sestamibi-imaging studies assessed both perfusion and wall motion abnormalities.

**Image interpretation**

For both MCE and G-SPECT, myocardial perfusion and wall motion were assessed in the same seven segments of left ventricle: apical, anterior, inferior, anteroseptal, inferoseptal, lateral and posterior. Images were classified as positive or negative for ischemia. A positive segment required a perfusion defect or a wall motion abnormality. The seven segments were divided into three areas corresponding to the three major coronary arteries. Anterior and anteroseptal segments to the left anterior descending artery, inferior and inferoseptal segments to right coronary artery and lateral and posterior segments to circumflex artery. The apical segment could be allocated with any artery, but when the apical segment was compromised lonely, the left anterior descending artery was considered responsible for the ischemic event. When, after coronary angiography, the patient had left domination, the inferior segment was allocated to circumflex artery.

**Enzyme determination**

Creatine phosphokinase-MB isoenzyme levels were measured after 6 and 12 hours of the beginning of chest pain, and if elevated, four times daily for the first 48 hours. An acute myocardial infarction was documented by an increase of CKMB greater than twice the normal value.

**Coronary angiography**

Selective coronary angiography was performed in multiple projections by the Judkins or Sones technique. Significant coronary artery disease was defined as ≥70% stenosis in a major coronary artery or its branches or ≥50% left main coronary artery stenosis. Stenoses of large diagonal or marginal branches were considered lesions of the left anterior descending or circumflex coronary artery, respectively. When a bypass graft was present, significant coronary artery disease was diagnosed if a stenosis was present in the graft or the grafted coronary artery that compromised distal blood flow.

**SPECT stress test**

Patient with negative findings in both MCE and G-SPECT were submitted to a myocardial perfusion imaging exercise tolerance test or dipyridamole test. When non-evidence of ischemia was documented the diagnosis of coronary artery disease was excluded. Otherwise, the patient underwent a coronary angiography.

**Final diagnosis**

The final diagnosis of an acute coronary event was made in the presence of positive findings in MCE or G-SPECT and the presence of significant obstructive coronary artery disease in the corresponding territory.

**Data analysis**

Sensitivity, specificity, negative and positive predictive values were determined using standard definitions. Chi-square testing with Fisher’s exact test was used for categorical variables, and Student’s t-test was used for continuous data. Kappa statistics were calculated for determination of concordance between MCE and G-SPECT. K of ≤0.4, >0.4 and
>0.7 indicate fair, good and excellent agreement, respectively\(^1\). Statistical significance was considered for p<0.05.

**Results**

**Clinical profile**

Six patients (33.3%) were determined to have had an ACE. In 12 patients (66.6%) ACE was excluded. The two groups could not be differentiated based on age, gender, duration of pain and free pain interval, as well as presence of risk factors and antecedents (Table 1).

**Table 1: Comparison of patients with and without an acute coronary event**

<table>
<thead>
<tr>
<th></th>
<th>ACE + (n=6)</th>
<th>ACE (n=12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.7±14.7</td>
<td>53.9±10.4</td>
<td>0.09</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>2/2</td>
<td>6/6</td>
<td>0.63</td>
</tr>
<tr>
<td>Duration of pain (min)</td>
<td>137.5±82.9</td>
<td>189.1±138.5</td>
<td>0.41</td>
</tr>
<tr>
<td>Pain free period (min)</td>
<td>155.0±95.6</td>
<td>122.5±75.9</td>
<td>0.44</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5 (83.3%)</td>
<td>6 (50.0%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (16.6%)</td>
<td>2 (16.6%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Elevated cholesterol</td>
<td>3 (50%)</td>
<td>7 (58.3%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>3 (50%)</td>
<td>1 (8.3%)</td>
<td>0.08</td>
</tr>
<tr>
<td>(+) family history</td>
<td>3 (50%)</td>
<td>2 (16.6%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>0 (0%)</td>
<td>1 (8.3%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>1 (16.6%)</td>
<td>2 (16.6%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

ACE +: acute coronary event present; ACE -: acute coronary event absent; CABG: coronary artery bypass graft; PTCA: percutaneous transluminal coronary angioplasty.

**Segment-by-segment analysis**

Of the 126 possible segments (7 per patient), wall motion analysis was performed in all and perfusion analysis was performed in 124. In two segments, perfusion could not be analyzed by MCE.

Concordance between two tests for evaluation of wall motion abnormalities showed a κ coefficient of 0.40. Concordance between two tests for evaluation of perfusion defects showed a κ coefficient of 0.04 (Figure 1).

**Acute coronary event diagnosis**

Sensitivity and specificity for G-SPECT were, respectively: 1.perfusion scores: 100 and 75%; 2.wall motion scores: 66 and 91.6%; 3. association perfusion+wall motion: 66 and 91.6%.

**Figure 1: Agreement between myocardial contrast echocardiography and gated single-photon emission tomography. A) perfusion scores; B) wall motion scores.**

A)  

<table>
<thead>
<tr>
<th></th>
<th>Echo (+)</th>
<th>Echo (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mibi (+)</td>
<td>1 (0.8%)</td>
<td>12 (9.7%)</td>
</tr>
<tr>
<td>Mibi (-)</td>
<td>5 (4.0%)</td>
<td>106 (85.5%)</td>
</tr>
</tbody>
</table>

Kappa=0.04

B)  

<table>
<thead>
<tr>
<th></th>
<th>Echo (+)</th>
<th>Echo (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mibi (+)</td>
<td>4 (3.2%)</td>
<td>5 (3.9%)</td>
</tr>
<tr>
<td>Mibi (-)</td>
<td>4 (3.2%)</td>
<td>113 (89.7%)</td>
</tr>
</tbody>
</table>

Kappa=0.04

**Figure 2: Sensitivity and Specificity of G-SPECT and MCE for the diagnosis of acute coronary event**

G-SPECT: gated 99mTc-sestamibi single-photon emission computed tomography; MCE: myocardial contrast echocardiography; P: perfusion; WM: wall motion. P = perfusion; WM = wall motion.

Negative and positive predictive values for G-SPECT were, respectively: 1.perfusion scores: 100 and 66%; 2.wall motion scores: 84.6 and 80%; 3. association perfusion+wall motion: 84.6 and 80%.

Negative and positive predictive values for MCE were, respectively: 1.perfusion scores: 71.4 and 50%; 2.wall motion scores: 71.4 and 50%; 3. association perfusion+wall motion: 68.7 and 0% (Table 2).
Table 2: Sensitivity, Specificity, Negative Predicted Value and Positive Predicted Value of G-SPECT and MCE for the diagnosis of acute coronary event

<table>
<thead>
<tr>
<th></th>
<th>G-SPECT</th>
<th>G-SPECT WM</th>
<th>G-SPECT P+WM</th>
<th>MCE</th>
<th>MCE WM</th>
<th>MCE P+WM</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENSITIVITY (%)</td>
<td>100,0</td>
<td>66,0</td>
<td>66,0</td>
<td>20,0</td>
<td>33,3</td>
<td>0</td>
</tr>
<tr>
<td>SPECIFICITY (%)</td>
<td>75,0</td>
<td>91,6</td>
<td>91,6</td>
<td>76,0</td>
<td>83,3</td>
<td>84,6</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>100,0</td>
<td>84,6</td>
<td>84,6</td>
<td>71,4</td>
<td>71,4</td>
<td>68,7</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>66,0</td>
<td>80,0</td>
<td>80,0</td>
<td>50,0</td>
<td>50,0</td>
<td>0</td>
</tr>
</tbody>
</table>

NPV: negative predicted value; PPV: positive predictive value; G-SPECT: gated 99mTc-sestamibi single-photon emission computed tomography; MCE: myocardial contrast echocardiography; P: perfusion; WM: wall motion.

Discussion

Appropriate triage of emergency room patients with chest pain and a normal or nondiagnostic ECG is difficult. ECG and cardiac markers do not have enough accuracy to exclude myocardial ischemia. Hospital admissions of many patients whose symptoms are ultimately attributed to nonischemic causes lead to an unnecessary spend of money 15.

We found that rest 99mTc–sestamibi can reliably identify patients with an acute coronary event among those who are admitted with chest pain at emergency room. Myocardial contrast echocardiography showed less applicability in this setting.

All patients but one underwent MCE and G-SPECT after a median of 2 hours of pain relief; and perfusion analysis of G-SPECT showed a sensitivity of 100%. Many studies found that sensitivity of SPECT was high for diagnosing significant disease in patients injected 2 to 6 hours of pain relief 3, 7.

In other hand perfusion analysis with MCE showed low sensitivity and negative predictive value to identify patients with significant coronary disease. This difference in the ability of MCE and G-SPECT reflected in the fair concordance between both methods.

G-SPECT and MCE assess perfusion by different ways. The scintigraphy technique involves cellular uptake of 99mTc–sestamibi, which is concentrated in mitochondria and depends of cellular integrity 16. MCE evaluates perfusion by infusion of microbubbles and analysis of coronary microcirculation 17.

As MCE and G-SPECT were performed after pain relief, coronary blood flow could be restored. Ischemia occurs under baseline conditions only when there is relatively severe stenosis of the epicardial vessel and baseline flow does not decrease until there is 80 to 85% narrowing of the vessel diameter 18. The persistence of perfusion defects in G-SPECT even after cessation of symptoms and return of coronary flow can be explained by myocardial stunned 19.

The analysis of wall motion by both methods were not enough sensitivity to exclude an acute coronary event. It has been demonstrated that echocardiography was insensitivity to exclude myocardial ischemia after pain relief 20.

Left ventricular dysfunction is an early marker of acute transient ischemia but it can reverse so early to be documented after pain relief. During coronary angioplasty, a brief period of ischemia induces myocardial dysfunction that normalizes after 30 seconds of reperfusion 21. When the ischemia period is more prolonged, over 5 to 7 minutes, the myocardial dysfunction maintain for 24 to 36 hours 22.

Furthermore, the ability of echocardiogram to detect wall motion dysfunction depends of the area affected. If less than 20% of myocardial thickening are compromised the myocardial function can be normal. In case of an acute myocardial infarction the echocardiogram can detect myocardial dysfunction when >5% of ventricular mass is compromised 23.

Conclusions

We concluded that myocardial perfusion imaging using 99mTc sestamibi in low risk patients with nondiagnostic ECG can successfully identify acute cardiac event. The myocardial contrast echocardiography, by the technique used, did not show enough accuracy to detect myocardial ischemia.

References

1. Lee TH, Cook EF, Weisberg M, Sargent RK, Wilson C, Goldman L. Acute chest pain in the emergency room:


