*Nuclear Medicine*

# Value of ECG-gated Thallium-201 Dipyridamole SPECT in Borderline Cases of Myocardial Perfusion Scan

*Yueh-Chung Chen,[1] Kun-Chou Chin[2] and Jing Tang Ko[3]*

***Background:*** Thallium-201 myocardial perfusion scan is a commonly utilized method for detection of coronary artery disease. Although this technique is generally reliable, results can be inconclusive in some cases. The purpose of this study was to assess whether candidates for coronary angiogram could be better identified with the addition of an electrocardiographic (ECG)-gated myocardial perfusion scan to a thallium scan.

***Method:*** A total of 512 patients with suspected coronary artery disease were included in this study and received a thallium scan. In 69 patients, the results were borderline, and 32 of these 69 patients also received an ECG-gated scan and underwent coronary angiogram within one month.

***Results:*** We found that 21 of the 32 patients who underwent coronary angiogram had significant coronary artery disease. However, when an ECG-gated perfusion scan was also performed, 25 of the 32 patients had abnormal regional wall motion following the stress test. Twenty-one of these 25 patients were found to have significant coronary artery disease. Statistical analysis revealed that the ECG-gated perfusion scan in combination with the thallium scan was significantly more accurate than the thallium scan alone in borderline cases of myocardial perfusion scan ($p = 0.0166$), with 100% sensitivity, 63.6% specificity, an 84% positive predictive rate, and a 100% negative predictive rate.

***Conclusions:*** The ECG-gated perfusion scan in combination with a thallium scan was more accurate in predicting the presence of coronary artery disease than a thallium scan alone in borderline cases of myocardial perfusion scan.

**Key Words:** Gated myocardial SPECT • Thallium-201 • Myocardial perfusion scan • Stunning • Coronary artery disease

## INTRODUCTION

Thallium-201 myocardial perfusion single-photon emission computed tomography (SPECT) is a commonly utilized method to detect coronary artery disease.[1] Although this technique is generally reliable, inconclusive results can be obtained when trying to detect perfusion defects involving a small territory,[2] reverse redistribution,[3] or fixed defects caused by an attenuation effect[4,5] (e.g. a diaphragm shadow in males or a breast shadow in females). The electrocardiographic (ECG) gated myocardial perfusion scan is utilized for assessment of regional and global motion of the left ventricular wall. This test may also be useful in differentiating attenuation artifacts from myocardial scars.

The purpose of this study was to assess the efficacy of performing an ECG-gated perfusion scan in combination with a thallium scan. We hypothesized that the

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1Division of Cardiology, Department of Internal Medicine, Taipei City Hospital, Ren-Ai Branch, [2]Department of Nuclear Medicine, Min-Sheng General Hospital, and [3]Division of Cardiology, De- partment of Internal Medicine,Taipei City Hospital, Zhong-Xiao Branch.
Address correspondence and reprint requests to: Dr. Yueh-Chung Chen, Division of Cardiology, Department of Internal Medicine, Taipei City Hospital, Ren-Ai Branch, No. 10, Section 4, Ren-Ai Road, Taipei 106, Taiwan. Tel: 886-2-2709-3600 ext. 3741; Fax: 886-2-2704-9399; E-mail: chenyuehchung.tw@yahoo.com.tw

combination of the two tests could help to clarify inconclusive results from a thallium scan,[6,7] and be useful in determining if an invasive coronary angiogram was needed.

## METHODS

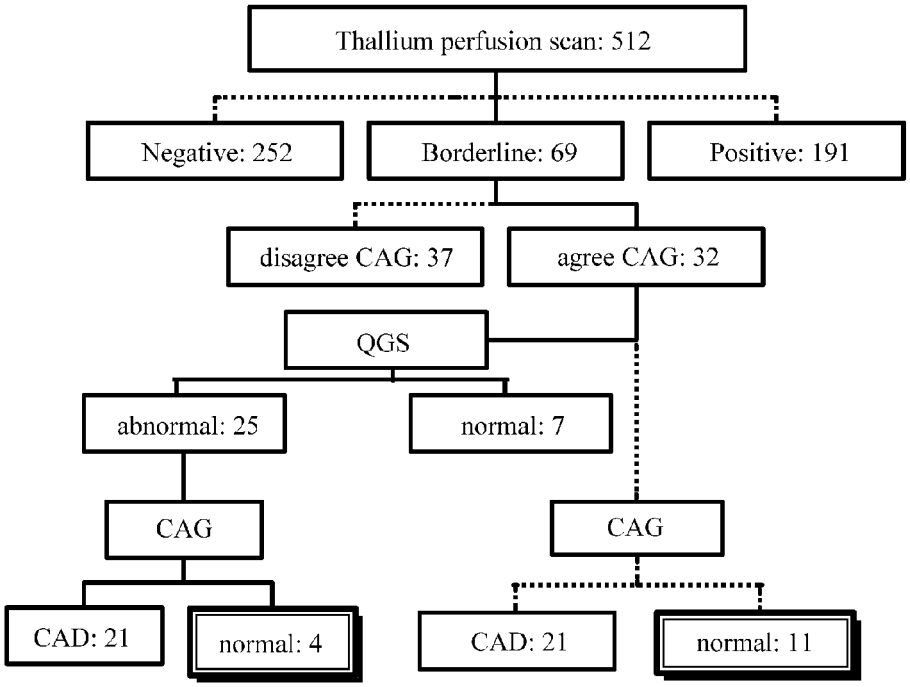
### Patient Population

From January to November of 2004, 512 patients in Ren-Ai Hospital with suspected coronary artery disease were included in the study and underwent stress thallium-201 myocardial perfusion SPECT. Exclusion criteria included a history of documented myocardial infarction, coronary bypass surgery, or percutaneous coronary intervention. A positive result was defined as a perfusion defect in an area larger than 6% of the total left ventricle with the exception of the inferior wall in male patients, the anterior wall in female patients, or areas with uptake reduced by 65%. A negative result was defined as no pre- or post-stress perfusion defect. Borderline results were defined as areas of reversible redistribution smaller than 6% of the total left ventricle, or areas of the inferior wall in male patients and anterior wall in female patients with 65% to 75% reduced uptake. According to these definitions, 191 patients had a positive result, 252 patients had a negative result, and 69 patients had a borderline result. All borderline case received ECG-gated scan simultaneously. Of the 69 cases with a borderline result, 32 patients received a coronary angiogram within one month of the scan. Of the 32 cases received angiogram, there were 44% women and 56% men with a mean body weight of 64 ± 16 kilogram and a mean age of 61 ± 14 years. Of the 69 cases with a borderline result, there were 41% women and 59% men with a mean body weight of 62 ± 14 kilogram and a mean age of 62 ± 15 years.

We selected 32 patients who underwent a coronary angiogram for further evaluation in order to assess if use of an ECG-gated scan was useful in clarifying inconclusive results of a thallium scan and identifying patients for an invasive coronary angiogram in clinical practice (Figure 1).

### Procedure

All patients were scanned in the supine position.




*CAG: coronary angiogram; QGS: Quantitative Gated SPECT.
*The numeral indicates the patient population.

***Figure 1.*** *Algorithm of the examination procedure.*

Dipyridamole 0.56 mg/kg was intravenously injected, and patients were instructed to raise each leg or do a handgrip maneuver as the adjuvant stress exercise. This was followed by injection of 2.5-3.0 mCi of thallium-201 followed by SPECT imaging. Imaging at rest was conducted after 3-4 hours.

The scintigraphic imagines were acquired with an ADAC dual-head SPECT camera (ADAC Laboratories, Milpitas,CA) equipped with a low-energy, high-resolusion collimator. Thirty-two projections (40 seconds perprojection) were obtained over a 180° semicircular arc (45° right anterior oblique to 45° left posterior oblique). Image resolution was 64 × 64 pixels. Filtered back projection was performed by use of a low-pass Butterworth filter with a frequency cutoff of 4 and an order of 5.

An ECG R wave gating detector was used to acquire 8 frames of each cardiac cycle. No attenuation or scatter correction was used. ECG-gated SPECT images were visually scored for motion using a 20-segment model of the left ventricle (Figure 2). Five representative slices (3 distal, middle and basal short-axis slices and 1 vertical and 1 horizontal mid-ventricular long axis slice) were automatically selected for this purpose.

All images were processed and interpreted by the same experienced technologist. All stress and rest images were displayed simultaneously on an ADAC Pegasys workstation (ADAC Laboratories) through use of the commercially available Autoquant QGS (Quantitative Gated SPECT) software program.[8,21] Images were analyzed using a linear color scale, with each color transition representing a 10% difference in uptake activity. Regional wall motion in the left ventricle was scored using a 20-segment model following the stress test.

### Statistical Analysis

Differences in data among two protocols were tested using analysis of standard deviation. The hypothesis test about the difference between two population propositions was used to evaluate the significance of successful examinations, using thallium scan alone or with the addition of the ECG-gated scan for detection of coronary artery disease. The level for statistical significance was predetermined at $p < 0.05$. All comparisons were one-tailed.

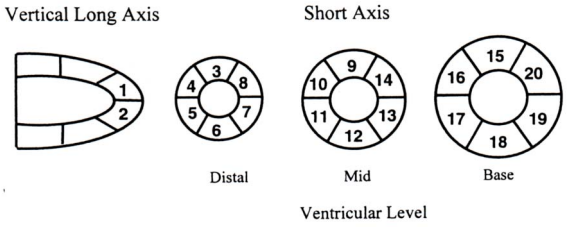



***Figure 2.*** *Schematic representation of the 20-segment model of the left ventricle.*

## RESULTS

We identified 69 patients with a borderline result on the thallium scan, and 32 of these patients underwent a coronary angiogram within one month following the scan. Of the patients undergoing a coronary angiogram, 21 of 32 patient exhibited significant coronary artery disease (> 50% stenosis of one or more vessels) and the remaining 11 patients showed normal or insignificant coronary artery disease. However, if ECG-gated perfusion scan was used simultaneously, 25 of the 32 patients exhibited abnormal regional wall motion following the stress test. Furthermore, 21 of these 25 patients exhibited significant coronary artery disease, with the remaining 4 patients exhibiting no coronary artery disease. Finally, 7 of the 32 patients with normal regional wall motion following the stress test exhibited normal or insignificant coronary artery disease.

Statistical analysis revealed that the ECG-gated perfusion scan in combination with the thallium scan was significantly more accurate than the thallium scan alone in borderline cases of myocardial perfusion scan ($p = 0.0166$), with 100% sensitivity, 63.6% specificity, an 84% positive predictive rate, and a 100% negative predictive rate. Patient data and characteristics are presented in Table 1.

## DISCUSSION

The post-stress perfusion defects caused by myocardial ischemia are similar to the so-called phenomena of transient ischemia stunning (TIS), indicating that the defects may be both transient and reversible.[9] The technique of technetium-99m SPECT offers a superior image quality compared to thallium-201 SPECT due to a higher

**Table 1.** Data from cases with borderline thallium-201 SPECT results

| Patient | sex | Age | BW (kg) | Perfusion scan | Post-stress LVEF (%) | Resting LVEF (%) | Regional wall motion abnormality after exercise (among 20 segments of left ventricle, Figure 2) | Coronary angiogram (stenotic vessels) |
|---|---|---|---|---|---|---|---|---|
| 1 | F | 57 | 55 | RR at anterior wall | 76 | 66 | 1, 19 | LAD, RCA |
| 2 | M | 58 | 69 | RR at anterior wall | 74 | 62 | 1, 8 | LAD, RCA |
| 3 | M | 66 | 69 | Small (5%) at inferolateral wall | 80 | 79 | 1, 8, 18 | RCA, LAD, LCX |
| 4 | M | 70 | 73 | Fixed inferior wall | 81 | 82 | 8, 10 | RCA |
| 5 | M | 65 | 64 | Small (2%) at inferolateral wall | 79 | 71 | 8, 13 | RCA |
| 6 | F | 51 | 44 | RR at inferior wall | 80 | 77 | 4, 6 | LCX, RCA |
| 7 | F | 66 | 69 | Small (5%) at inferior, inferolateral wall | 81 | 87 | 1, 4, 5, 6, 8 | RCA, LAD, LCX |
| 8 | M | 72 | 71 | Small (5%) at inferolateral wall | 82 | 75 | 18, 19 | RCA, LAD, LCX |
| 9 | F | 51 | 58 | RR at inferior, inferolateral wall | 84 | 75 | 1, 3, 8 | LAD |
| 10 | F | 70 | 55 | RR at anteroseptum | 76 | 78 | 1, 4, 8, 10 | LAD, RCA |
| 11 | F | 66 | 50 | RR at anteroseptum, inferior wall | 45 | 40 | global hypokinesis | LAD, LCX |
| 12 | F | 47 | 73 | Fixed anterior wall | 65 | 63 | 1, 9, 10, 14 | LAD |
| 13 | M | 75 | 69 | Small (4%) at anterior wall | 60 | 68 | 1, 3, 8 | LCX, LAD |
| 14 | F | 46 | 70 | Fix anterior wall defect | 60 | 59 | 3, 8 | RCA |
| 15 | M | 69 | 73 | Small (4%) at anterior wall | 55 | 51 | 1, 3, 9, 14 | LAD |
| 16 | M | 61 | 60 | Fixed inferior defect | 49 | 57 | 6, 7, 10 | RCA |
| 17 | M | 57 | 68 | RR at anteroseptum | 63 | 66 | 4, 10 | LAD |
| 18 | F | 71 | 54 | RR at anterior wall, inferoseptum | 66 | 54 | 19 | LCX |
| 19 | M | 66 | 62 | Fixed hypoperfused inferolateral wall | 46 | 58 | 1, 18 | RCA |
| 20 | F | 51 | 58 | RR at inferior wall | 60 | 53 | 6, 7, 8 | RCA |
| 21 | M | 72 | 67 | Small (1%) at anterior wall | 66 | 60 | 8, 9,14 | LAD |
| 22 | M | 59 | 66 | RR at inferior wall, inferoseptum | 70 | 65 | 8, 12 | Negative |
| 23 | F | 54 | 80 | RR at inferoseptum | 75 | 75 | 4, 8, 10. | Negative |
| 24 | M | 63 | 78 | RR at inferior wall | 60 | 53 | 4, 5, 6 | Negative |
| 25 | M | 57 | 69 | Small (2%) at apicoanterolateral region | 74 | 69 | Normal | LCX insignificant stenosis |
| 26 | M | 53 | 79 | Small (5%) at anterior wall | 65 | 59 | Normal | Negative |
| 27 | F | 42 | 44 | RR at inferior wall | 45 | 40 | 6, 12 | Negative |
| 28 | M | 70 | 62 | Fixed hypoperfused inferior wall | 63 | 57 | Normal | Negative |
| 29 | M | 74 | 71 | Fixed inferior wall | 61 | 58 | Normal | Negative |
| 30 | M | 73 | 64 | RR at inferior wall, septum wall | 76 | 58 | Normal | Negative |
| 31 | F | 42 | 54 | RR at inferoseptum | 68 | 52 | Normal | Negative |
| 32 | F | 60 | 56 | RR at anterior wall | 78 | 86 | Normal | Negative |

*RR: reversible redistribution; LAD: left anterior descending artery; LCX: left circumflex artery, RCA: right coronary artery.

density and less likelihood of borderline results. However, technetium-99m SPECT is performed with delayed imaging and may have some pitfalls with respect to TIS detection.[10,11] Thallium-201 SPECT imaging, on the

other hand, is better suited for TIS detection[12] but has a higher rate of borderline results.[13,14] Reverse redistribution in a resting thallium scan in patients with coronary artery disease also has a close relationship with coronary anatomy and ventricular function.[15] However, the anatomic correlation in our study seemed not very identical. We believed this is not uncommon in clinical practice.

The addition of an ECG-gated scan to technetium-99m scan can clarify the uncertainty of borderline results and increase the success rate of diagnosing coronary artery disease.[16] Gated SPECT imaging is also of value in recognizing questionable perfusion defects,[4] including attenuation artifacts, which are ubiquitous, particularly when persistent defects raise the question of myocardial scar versus defect. The presence of corresponding normal or abnormal wall motion before and after stress imaging with an ECG-gated scan may resolve this problem, and may be even more accurate than the treadmill exercise test (The change of regional wall motion observed by echocardiography pre- and post-stress may be more accurate than treadmill exercise test[22] for the diagnosis of coronary artery disease). The complementary information can also be useful to evaluate the severity of TIS and the extent of myocardial viability. Furthermore, the ejection fraction of the left ventricle can be accurately assessed by gated SPECT with either technetium-99m or thallium scan in properly selected patients (e.g. patients who are not overweight) with normal or depressed left ventricular function.[17,18] Assessment of global function is useful for determing prognosis and in differentiating ischemic from non-ischemic cardiomyopathy.[19]

In the current study, we evaluated the efficacy of coronary artery disease detection by using the same QGS (Quantitative Gated SPECT) method in combination with a thallium scan. Based on the findings of the coronary angiograms, more than half of the borderline cases identified by thallium scan revealed significant coronary artery disease, indicating the value of following the borderline cases with a coronary angiogram. However, our study showed, if QGS (e.g. ECG-gated scan) was added in these borderline cases, the coronary artery disease detection rate by coronary angiogram increased. These findings suggest that borderline patients with abnormal presentation following QGS should receive an angiogram.

There remains a number of issues that require further clarification, including the diagnostic value of QGS when the thallium scan is positive or when the thallium scan is negative. We believe that ECG-gated SPECT also improves diagnosis in those populations, and that will be the subject of further investigation.

Finally, we should note that our study has some limitation. Minimal bias may still exist in the interpretation even though we used the same experienced technologist. Besides, there was no absolute standard for determining the contribution of collateral flow to regions with an anatomic obstruction. Furthermore, these catheterized patients were not randomly selected, and the total number of cases examined was relatively small.

## CONCLUSION

The addition of an ECG-gated perfusion scan may reduce the uncertainty in interpreting results of a thallium scan alone, especially with respect to interpretation of borderline results. Measuring resting and post-stress left ventricular ejection fraction and changes in regional wall motion,[7,20] can make it possible to detect coronary artery disease more precisely in clinical practice.

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# 心節律門閥鉈壓力攝影對傳統造影邊緣型病例之價值

陳鉞忠[1] 秦公焯[2] 柯景塘[3]
台北市 市立聯合醫院仁愛分院 心臟內科[1]
桃園縣 敏盛醫院 核子醫學科[2]
台北市 市立聯合醫院忠孝分院 心臟內科[3]

**背景** 鉈-201 心肌灌注攝影為一常用於冠心症診斷之工具，然而常有一些情形，例如小區域之缺氧、可逆性再分佈及衰減效應造成之灌流不足，均可能使判讀發生困難。

**方法** 我們希望使用心節律門閥鉈壓力攝影加入原來檢查顯示邊緣性結果之病例中，看是否可以增加冠心症之正確診斷。2004 年 1 月至 11 月共 512 位受檢病人中，有 69 位呈現邊緣性結果，其中 32 位接受了心導管檢查，本實驗即取此 32 名病例做分析。

**結果** 鉈-201 心肌灌注攝影 32 名邊緣性病例中，21 位有顯著冠心症，11 位無；此 32 名病例若再加上心節律門閥鉈壓力攝影檢查後，不正常變化之病例共 25 位，當中 21 位有顯著冠心症，4 位無，而無不正常變化之 7 名病例中均無冠心症；換言之，本研究從邊緣病例中，找出 32 名，將這 32 名病例皆實施心導管手術，其中有 11 名將被誤作心導管手術，但多加了一套檢驗手續，此 32 名病例中僅 4 名可能被誤作心導管手術，可見後者比前者更能降低誤判的機率。我們使用兩母體比率差異之假設檢驗來測試此一結果，顯示假設有意義，$p$ 值 $= 0.0166$ ($p < 0.05$)。

**結論** 心節律門閥鉈壓力攝影對鉈-201 心肌灌注攝影邊緣性結果之病人，於冠心症之診斷上有極佳的參考效果。

**關鍵詞：**心節律門閥鉈壓力攝影、鉈-201、心肌灌注攝影、心肌昏迷、冠心症。