Correlation between Myocardial Perfusion Imaging Findings and Cardiac Events

Arpakorn Kositwattanarerk MD*,
Chanika Sritara MD*, Piyamit Sritara MD**

** Nuclear Medicine Division, Department of Radiology, Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand*
*** Cardiology Unit, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand*

Objective: *The excellent prognostic value of a normal or near normal stress myocardial perfusion imaging (MPI) has been confirmed in numerous studies. The aim of the present study was to determine the association of MPI findings and cardiac events.*
Material and Method: *Consecutive patients referred from January 2003 to December 2004 by Nuclear Medicine Unit in Ramathibodi Hospital for myocardial perfusion imaging were studied. Visual scoring of perfusion images used 17-segments and a scale of 0-4 was done. Sum stress score (SSS) was generated. Cardiac death, death from any cause and nonfatal acute myocardial infarction (MI) were considered major cardiac events, and chest pain and late revascularization > 60 days after testing were considered minor cardiac events.*
Results: *Of the 320 patients studied, 218 subjects who had complete 1-year follow-up, were enrolled. There were 99 patients with normal MPI (SSS $\leq$ 3) and 119 patients with abnormal MPI (SSS > 3). Statistical significance between cardiac events in two groups ($p < 0.001$) was detected. Among hard events, there were three cardiac deaths (of these, 1 occurred in a patient with normal MPI and 2 in those with abnormal MPI) and no patients had non-fatal MI in both groups. Among minor cardiac events, 17 patients developed chest pain and 11 patients underwent late revascularization. No patient with normal MPI underwent revascularization (included early and late revascularization) was found.*
Conclusion: *These results show that SSS can be used to provide incremental prognostic information beyond clinical data, which confirms the conclusions drawn from the results of previous studies by using nuclear stress test results.*

Keywords: *Myocardial perfusion imaging, Cardiac events*

J Med Assoc Thai 2009; 92 (11): 1470-5
Full text. e-Journal: *http://www.mat.or.th/journal*

From the previous studies of patients that underwent nuclear stress testing, clinical factors contributed most of the prognostic information, while the sum stress score (SSS) provided substantial additional prognostic information beyond those baseline clinical predictors for each of the outcomes[1-6]. The excellent prognostic value of a normal or near normal stress myocardial perfusion imaging (MPI) has been confirmed in numerous studies[7-11] using various radiopharmaceutical agents, stress modalities (exercise versus pharmacologic), or pharmacologic stress agent used (dipyridamole, adenosine or dobutamine).

There is no previous study about MPI result and cardiac events at Ramathibodi Hospital. The aim of the present study was to determine the association of MPI result and cardiac events. The major cardiac events include cardiac death, death from any cause and nonfatal acute myocardial infarction (MI). The minor cardiac events comprised of chest pain and late revascularization (> 60 days after testing). The former studies were found that patients who undergo revascularization within the first 60 days after nuclear testing tend to do so, in part, based on their scan results, whereas patients referred to revascularization

Correspondence to: Kositwattanarerk A, Nuclear Medicine Division, Department of Radiology, Faculty of Medicine, Ramathibodi Hospital, Rama 6 Rd, Bangkok 10400, Thailand. Phone: 0-2201-1157, Fax: 0-2201-1191. E-mail: kung13521@hotmail.com

> 60 days after nuclear testing tended to be referred because of worsening of their clinical status[4,6].

Material and Method

The present study included the patients referred between January 2003 and December 2004 by Nuclear Medicine Unit in Ramathibodi Hospital for a study on myocardial perfusion imaging. The patients who underwent only rest-redistribution study without stress were excluded from the present study.

Stress-rest myocardial perfusion study protocol

Exercise stress test

Patients who were capable of exercising underwent an exercise treadmill stress test. Blood pressure, heart rate, and a continuous 12-lead electrocardiogram were monitored throughout the stress portion of the test and into the recovery phase. The radiopharmaceutical agent (^{99m}Tc-MIBI or ^{201}Tl) was injected about 1 minute before conclusion of the exercise. The examination was considered to be terminated due to chest pain, achieved target heart rate (85% of maximum age-predicted heart rate), EKG changed (horizontal or downsloping ST-segment depression > 2 mm at 80 ms after the J-point) or abnormal hemodynamic response.

Pharmacologic stress test

Patients who were unable to exercise or who had clinical contraindications to exercise underwent a pharmacologic stress test with one of two agents: dobutamine or dipyridamole.

Dipyridamole was administered intravenously at an infusion rate of 0.142 mg/kg/min for 4 minutes. The radiopharmaceutical was administered 3 minutes after completion of the infusion. Intravenous aminophylline (125 mg) was used to reverse dipyridamole-induced side effects.

Dobutamine, an intravenous infusion of dobutamine was initiated at a rate of 5 mg/kg/min for 3 minutes and increased at a rate of 5 mg/kg/min every 3 minutes until a target heart rate was reached. The examination could be terminated because of patient symptoms, evidence of significant ischemia, prolonged arrhythmias, or when the dobutamine infusion rate reached a maximum rate of 40 mg/kg/min. The radiotracer was injected when one of the previously mentioned end points was reached.

The patients were immediately scanned (less than 15 minutes) after injection of ^{201}Tl but the patients who were injected with ^{99m}TcMIBI have to wait for 30-60 minutes and eat a fatty meal before the scan.

Rest

Isordil 5 mg was given orally 20 minutes before radiopharmaceutical injection.

Single Photon Emission Computed Tomography (SPECT) images were acquired and processed with single head gamma camera (FORTE, ADAC laboratory) and 180° acquisition for 32 projections at 30 seconds per projection. Low-energy, high-resolution collimator was used.

During imaging, two energy windows were used for ^{201}Tl, including a 20% window centered on the 71 keV peak and 167 keV peak. For ^{99m}Tc-MIBI, a 20% window centered on the 140 keV peak was used. No attenuation or scatter correction was used. Processing images by technologist was acquired using Butterworth filter and Autoquant program.

Image analysis

Images were interpreted by an experienced nuclear medicine physician.

All of the patients in the present study were defined a summed stress score using a 17-segment scoring system with 5-point severity scale. The 17-segment scoring system, as shown in Fig. 1, was based on 3 short axis slices (apical, mid-ventricular, and basal) designed to signify the entire left ventricle, with the apex represented by 1 segment visualized in a mid-vertical long axis image. Each segment was scored as follows: 0 = normal; 1 = slight reduction of uptake (equivocal); 2 = moderate reduction of uptake (usually implies a significant abnormality); 3 = severe reduction of uptake; 4 = absence of radioactive uptake. A SSS was obtained by adding the scores of the 17 segments of the stress images.

Based on previous studies to determine the prognostic ability of SPECT perfusion studies, a

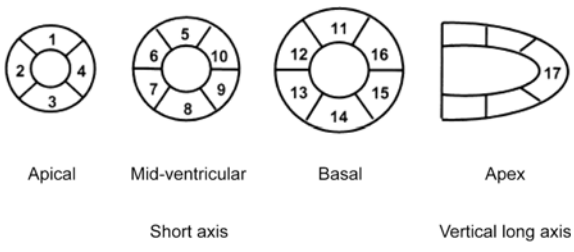

Fig. 1 Assignment of myocardial region for scoring the SPECT images

summed stress score ≤ 3 was considered the normal group and SSS > 3 was considered the abnormal group[12].

Data collection and management

The baseline data of the patients were reported by reviewing the patients' hospital chart.

Hypertension was defined as repeated BP measurements of >140/90 mmHg or intake of antihypertensive medication. Diabetes mellitus was defined as a fasting glucose level ≥ 7.8 mmol/L or the need for insulin or oral hypoglycemic agents. Hypercholesterolemia was defined as a total cholesterol of ≥ 6.4 mmol/L or treatment with lipid-lowering agents.

After performing MPI, the patients were divided in 2 groups. The normal group was considered when SSS ≤ 3 and the abnormal group was considered when SSS > 3.

Follow-up by review of the patient's hospital chart within 1 year after MPI was performed to identify cardiac events that included major cardiac events such as cardiac death, death from another cause and nonfatal acute MI, as well as minor cardiac events *i.e.* chest pain and revascularization.

Without information in the hospital chart, telephone interviews were conducted. Data were extracted and entered into data collection form. Cardiac death was defined as a death associated with a known or suspected acute MI, arrhythmia, or pulmonary edema. Sudden death without non-cardiac cause was also considered cardiac death. Non-fatal acute MI was defined by clinical symptoms with clinical, cardiac enzyme levels, and EKG changes. Only the patients who had chest pain severe enough to go to the emergency room or be admitted were counted for minor cardiac events. Revascularization included coronary artery bypass surgery, percutaneous coronary intervention, with stent and percutaneous transluminal coronary angioplasty.

Statistical analysis

Continuous variables are expressed as mean and standard deviation (SD). Patient groups were compared using student's t-test for continuous variables. Categorical data are expressed as proportions and were compared by the Chi-square and Fisher's Exact test. A p-value ≤ 0.05 was considered significant.

Results

Of the 320 patients studied, 218 patients who had complete 1-year follow-up, were enrolled. There were 88 men and 130 women. There were 99 patients with normal MPI (SSS ≤ 3) and 119 patients with abnormal MPI (SSS > 3). The clinical characteristics of the present study patients are demonstrated in Table 1. Mean age was 64.5 ± 12 years, and there were 88 men (40.37%) in the present study.

The information of myocardial perfusion imaging results is summarized in Table 2. The scan findings showed statistical difference between normal and abnormal groups as the following: left ventricular (LV) dilatation ($p < 0.001$), stress-induced LV dilatation ($p = 0.031$), abnormal lung uptake ($p = 0.04$) and abnormal wall motion ($p = 0.001$).

Cardiac events

Comparison of cardiac events between normal and abnormal MPI is illustrated in Table 3.

During the 1-year follow-up period, among major cardiac events, there were three cardiac deaths: one occurred in a patient with normal MPI, and two in those with abnormal MPI. There were no patients of non fatal acute MI in both groups. Among minor cardiac events, 17 events of chest pain were counted and 11 patients underwent late revascularization. However, no patients with normal MPI underwent revascularization (included early and late revascularization). From the present study, there was statistical difference of the cardiac events in two groups ($p < 0.001$).

Ninety-nine patients (45.41%) of the patients who were followed-up had a normal scan (SSS ≤ 3). There was only one death in this group and no patients had a MI during the entire follow-up. With regard to the minor cardiac events, only one patient had chest pain and no patient underwent late revascularization.

One hundred and nineteen patients (54.59%) of the patients who were followed-up had an abnormal scan (SSS > 3). Over the entire follow-up period, there were two deaths in patients with abnormal scans. No patients in this group developed non-fatal acute MI. With regard to the minor cardiac events, 16 patient developed chest pain and 11 patients underwent late revascularization.

Discussion

A normal SSS (0-3) was associated with a mortality of less than 1% whereas an increased SSS predicted an increased cardiac mortality. In a follow-up study of 5,183 patients that included patients with pharmacologic stress and exercise stress, Hachamovitch et al[1] confirmed their initial findings that SSS provided significant prognostic information

Table 1. Patient characteristics

Baseline characteristic (n = 218)	Normal imaging No. (%)	Abnormal imaging No. (%)	Total No. (%)	p-value
Sex				0.006
Male	30	58	88 (40.37)	
Female	69	61	130 (59.63)	
Age (year)	63.1 ± 12.41	65.7 ± 11.95	64.5 ± 12.2	0.110
DM	2/99 (2.02)	6/119 (5.04)	8/218 (3.67)	0.297
HT	19/99 (19.19)	16/119 (13.45)	35/218 (16.06)	0.250
DLP	6/99 (6.06)	4/119 (3.36)	10/218 (4.59)	0.518
CAD	1/99 (1.01)	14/119 (11.76)	15/218 (6.88)	0.002
DM + HT	10/99 (10.10)	12/119 (10.08)	22/218 (10.09)	0.997
DM + DLP	3/99 (3.03)	0/119	3/218 (1.38)	0.092
DM + CAD	0/99	2/119 (1.68)	2/218 (0.92)	0.502
HT + DLP	15/99 (15.15)	12/119 (10.08)	27/218 (12.39)	0.258
HT + CAD	3/99 (3.03)	7/119 (5.88)	10/218 (4.59)	0.354
DM + HT + DLP	5/99 (5.05)	18/119 (15.13)	23/218 (10.55)	0.016
DM + HT + CAD	3/99 (3.03)	5/119 (4.2)	8/218 (3.67)	0.647
HT + DLP + CAD	2/99 (2.02)	6/119 (5.04)	8/218 (3.67)	0.297
DM + HT + DLP + CAD	2/99 (2.02)	1/119 (0.84)	3/218 (1.38)	0.592

HT = hypertension, DM = diabetes mellitus, DLP = dyslipidemia, CAD = coronary artery disease

Table 2. Imaging results

Item	Normal imaging No. (%)	Abnormal imaging No. (%)	Total No. (%)	p-value
Tracer				0.127
MIBI	86/99(86.87)	94/119 (78.99)	180/218 (82.57)	
Tl	13/99(13.13)	25/119 (21.01)	38/218 (17.43)	
MPI interpretation				
LV dilatation at rest	9/99 (9.09)	36/119 (30.25)	45/218 (79.36)	0.000
Stress induce LV dilatation	21/99 (21.21)	41/119 (34.45)	62/119 (28.44)	0.031
Abnormal lung uptake	2/99 (2.02)	10/119 (8.40)	12/218 (5.50)	0.040
Gated SPECT				
No	13/99 (13.13)	21/119 (20.17)	37/218 (16.97)	
Yes	86/99 (86.87)	95/119 (79.73)	181/218(83.03)	
Abnormal wall motion	2/86 (2.32)	21/95 (22.10)	23/218 (10.55)	0.000
EF: ≥ 50%	35/86 (40.70)	45/95 (47.37)	80/218 (36.7)	0.167
< 50%	4/86 (4.65)	9/95 (9.47)	13/218 (5.96)	
No record	47/86 (54.65)	41/95 (43.16)	88/218 (40.37)	

MIBI = Sestamibi, Tl = Thallium , MPI = myocardial perfusion imaging , LV = left ventricular , EF = ejection fraction

beyond clinical variables ($p < 0.001$). Vanzetto et al[11] also found that myocardial perfusion imaging with ^{201}Tl provided significant prognostic information in addition to that provided by clinical variables and exercise stress tests ($p < 0.01$). The findings of Vanzetto included 6 years of follow-up compared with the shorter 1.5 and 1.75 years of follow-up in the studies of Hachamovitch. In a more recent cohort study, Borges-Neto et al[13] followed-up 1,818 consecutive patients who received MPI with ^{99m}Tc-MIBI or ^{99m}Tc-tetrofosmin and showed that SSS combined with clinical index was a significantly better model

Table 3. Cardiac events between normal and abnormal MPI

Event	Number incidence (%)		
	Normal MPI n = 99	Abnormal MPI n = 119	p-value
Major cardiac events			<0.001
Cardiac death	1/99	2/119	
Death from other cause	0/99	0/119	
Non fatal acute MI	0/99	0/119	
Minor cardiac events			
Chest pain	1/99	16/119	
Late revascularization	0/99	11/119	

than adjusting for only baseline characteristics for predicted endpoints ($p < 0.001$ for death from any cause, $p < 0.001$ for cardiovascular death and $p = 0.004$ for MI, respectively).

From the present study, there was statistical difference of the cardiac events in two groups ($p = 0.000$).

In the group of normal scan, one patient died. He had underlying coronary artery disease (CAD) and colon cancer. His previous Coronary Angiography (CAG) result (performed 1 month before MPI showed 30% stenosis of left main coronary artery (LM). MPI results showed mild perfusion at apical segment of anterior wall (SSS = 1). He underwent surgery about 6 months after performing MPI, and then lost follow-up from Ramathibodi Hospital. Data obtained from his daughter reported that he had chest pain and sudden death.

In groups of abnormal MPI, two patients died. The first patient had underlying CAD and presented with dyspnea. MPI result showed severe perfusion defects at apical segment of anterior wall and entire inferior wall (SSS = 12) and increase lung uptake with stress-induced LV dilatation. The second patient had previous CAG from a private hospital, which showed double vessel disease DVD: 70% stenosis of left anterior descending artery at proximal segment with collateral to right coronary artery (RCA), and total proximal occlusion and 75% distal occlusion of RCA). His previous echocardiogram revealed left ventricular ejection fraction of 37%. The MPI results showed moderate perfusion defects at apex, mid-ventricular segments of inferior and inferolateral walls, mild perfusion defects at apicoseptum, apical segment of inferior wall, basal segment of inferolateral wall, and mid-ventricular segment of anterolatral wall (SSS = 10).

In conclusion, the results of SPECT myocardial perfusion imaging provide important information that should influence the clinician in the decision-making process regarding appropriate therapy options, as well as help providers and patients understand the risk for future cardiac events.

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ความสัมพันธ์ระหว่างสิ่งตรวจพบจากภาพการกำซาบของกล้ามเนื้อหัวใจกับเหตุการณ์ทางหัวใจ

อาภากร โฆษิตวัฒนฤกษ์, ชนิกา ศรีธรา, ปิยมิตร ศรีธรา

วัตถุประสงค์*: ภาพการกำซาบของกล้ามเนื้อหัวใจที่เป็นปกติหรือเกือบปกติช่วยยืนยันว่า เป็นค่าทำนายที่ดีเลิศ ในหลายการศึกษา วัตถุประสงค์ของการศึกษาคือ ตรวจหาความสัมพันธ์ ระหว่างสิ่งตรวจพบจากภาพการกำซาบ ของกล้ามเนื้อหัวใจกับเหตุการณ์ทางหัวใจ*

วัสดุและวิธีการ*: ศึกษาในผู้ป่วยส่งต่อตามลำดับระหว่างเดือนมกราคม พ.ศ. 2546 ถึง เดือนธันวาคม พ.ศ. 2547 ทำโดยหน่วยเวชศาสตร์นิวเคลียร์ โรงพยาบาลรามาธิบดี เพื่อบันทึกภาพการกำซาบของกล้ามเนื้อหัวใจ มาตรวัดการเห็นภาพการกำซาบใน 17 ส่วนและระบุขีดคะแนนเท่ากับ 0 ถึง 4 ให้คะแนนความเหนื่อยรวม เหตุการณ์หัวใจหลักใหญ่ได้แก่ ตายจากโรคหัวใจ ตายจากสาเหตุอื่น และกล้ามเนื้อหัวใจขาดเลือดเฉียบพลัน โดยไม่เสียชีวิตส่วนเหตุการณ์หัวใจหลักรอง ได้แก่ เจ็บหน้าอก และการทำให้เลือดหล่อเลี้ยงได้อีกครั้งภายใน 60 วัน หลังจากการทดสอบ*

ผลการศึกษา*: ศึกษาและติดตามผลการรักษาอย่างสมบูรณ์นาน 1 ปี ในผู้ป่วย 218 ราย ในจำนวนทั้งหมด 320 ราย ผู้ป่วย 99 ราย ภาพการกำซาบของกล้ามเนื้อหัวใจปกติ 1 ปี การติดตามผู้ป่วยทำได้ 218 รายจากผู้ป่วยทั้งหมด 320 ราย มีผลการตรวจปกติ 99 รายและผิดปกติ 119 ราย พบว่ามีความแตกต่างกันอย่างมีนัยสำคัญ ในการเกิด อุบัติการณ์ทางหัวใจระหว่างผู้ป่วยทั้ง 2 กลุ่ม (p-value = 0.000) มีผู้ป่วยทั้งหมด 3 รายเสียชีวิตโดย 1 ราย มีผลการตรวจปกติ และ 2 รายมีผลการตรวจผิดปกติ ไม่มีผู้ป่วยรายใดมีกล้ามเนื้อหัวใจตายเฉียบพลัน ส่วนเหตุการณ์ หัวใจหลักรอง พบว่ามีผู้ป่วย 16 รายมีอาการเจ็บหน้าอกโดย 1 รายเป็นผู้ป่วยที่มีผลปกติ และ 11 รายได้ทำ late revascularization ซึ่งทุกคนมีผลการตรวจผิดปกติ*

สรุป*: การศึกษาการตรวจหัวใจโดยใช้สารเภสัชรังสี และอุบัติการณ์ทางหัวใจในกลุ่มผู้ป่วยของโรงพยาบาลรามาธิบดี พบว่าสามารถใช้คะแนนความเหนื่อยรวม บอกการพยากรณ์ได้ ซึ่งผลที่ได้สอดคล้องเหมือนการศึกษาก่อนหน้านี้*