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Original

Prediction of future cardiac events using myocardial perfusion SPECT: a middle-term follow-up study

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ABSTRACT

Background: Myocardial perfusion imaging (MPI) provides highly valuable information for risk stratification and determination of optimal clinical management. The goal of the present study was to assess the prognostic value of myocardial perfusion SPECT for the prediction of future cardiac events in Asian population.
Methods: Five hundred and ten consecutive patients, who had undergone myocardial perfusion SPECT between 2005 and 2006, were prospectively followed-up. Patients' data were collected from recorded files. Follow-ups were performed by scripted telephone interviews by a physician blinded to the patients' MPI results and also from the hospital records. The total completed follow-ups consisted of 482 patients (follow-up rate, 94.5%).
Results: Over the mean follow-up period of 434 ± 62 days, 14 out of 482 patients (2.9%) died from cardiac events. Also in 61 patients (12.7%), the clinical condition led to a cardiac intervention (Percutaneous coronary intervention or coronary artery bypass grafting). Those patients without cardiac events on follow-up (including cardiac death or myocardial infarction) were younger and with less severity of MPI abnormalities. Severe MPI abnormalities (Summed Stress Score > 13) were found in 42.9% of those with cardiac death, while in 17.2% of those with myocardial infarction. The rate of cardiac death had a direct relationship with the severity of scan abnormalities, however, the same association was not found between the severity of MPI abnormality and the rate of myocardial infarction.
Conclusion: MPI is a valuable tool for risk stratification and prediction of future fatal cardiac events in Asian population. The risk of cardiac death as a mid-term outcome of coronary artery disease increases significantly with severity of MPI abnormalities.

Predicción de eventos cardiacos futuros con SPECT de perfusión miocárdica: estudio de seguimiento a medio plazo

Palabras clave:
Imagen de perfusión miocárdica
SPECT
Sestamibi
Pronóstico
Eventos cardiacos
Enfermedad

RESUMEN

Introducción: Los estudios de perfusión miocárdica (MPI) aportan una importante información para la estratificación del riesgo y para determinar el óptimo manejo clínico del paciente. El objetivo del presente estudio es valorar el factor pronóstico de los estudios SPECT de perfusión miocárdica para predecir futuros eventos cardiacos en la población asiática.
Método: Se realizó un seguimiento prospectivo a 510 pacientes a los que se les realizó un estudio SPECT de perfusión miocárdica entre los años 2005-2006. Los datos de los pacientes se obtuvieron de los informes. El seguimiento se realizó mediante entrevista telefónica por un médico que desconocía los resultados del estudio MPI y los informes del hospital. Se completó el seguimiento en 482 pacientes (índice de seguimiento del 94,5%).
Resultados: Con un periodo de seguimiento medio de 434 ± 62 días, 14 de los 482 pacientes (2,9%) fallecieron por eventos cardiacos. En 61 paciente (12,7%) las condiciones clínicas requirieron de intervencionismo cardiaco (vasodilatación percutánea o bypass coronario). Aquellos pacientes sin eventos cardiacos en el seguimiento (incluyendo muerte cardiaca o infarto) eran más jóvenes y con alteraciones menos severas en MPI. Se encontraron alteraciones severas en los MOI (Summed Stress Score > 13) en el 42,9% de los pacientes con muerte cardiaca y en el 17,2% de los pacientes con infarto de miocardio. El índice de muerte cardiaca tuvo una relación directa con la severidad de las alteraciones en la gammagrafía, sin embargo, no se encontró esta relación con el índice de infartos.

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Conclusión: Los estudios de MPI tienen un valor clave en la estratificación del riesgo y en la predicción de eventos cardiaco fatales en el futuro en la población asiática. El riesgo de muerte cardiaca y la evolución a medio plazo de la enfermedad coronaria aumentan de forma significativa con la severidad de las alteraciones de MPI.

Introduction

Noninvasive imaging modalities can provide precious prognostic information useful in risk stratification and clinical management of patients with definite or probable coronary artery disease (CAD). The main goal of risk stratification in these patients is to distinguish patients at high risk for cardiac events (who may benefit from further invasive strategies) from low-risk patients (who do not require further invasive work up).[1–3] Thus, designation of patients to groups of low, intermediate, and high risk for cardiac events, including fatal or nonfatal myocardial infarction, unstable angina and sudden cardiac death, provides invaluable information in the management of these patients.[4]

Myocardial perfusion imaging (MPI) provides useful information for risk stratification and determination of optimal clinical management. In some populations, it has been shown that more extensive perfusion abnormalities are associated with the severity of CAD and a greater risk for life threatening cardiac events.[5] On the other hand, ethnic differences in clinical outcome of CAD exist. However, it is not known if risk scores derived from a specific ethnicity can accurately assess CAD risk in other populations.

The relationship between the findings of MPI and future cardiac events has not yet been shown previously in Asian population, comprehensively. Therefore, the goal of the present study was to highlight this relationship.

Methods

In the present study, 510 consecutive patients who were referred for myocardial perfusion SPECT to the Nuclear Medicine department of our hospital, during the year 2005 were enrolled. Demographic variables including age and gender, history of risk factors for CAD (Diabetes Mellitus, Hypertension, Dyslipidemia, and Cigarette Smoking), previous cardiac interventions and also the results of MPI were collected from the recorded files.

Myocardial perfusion scan

All myocardial perfusion SPECT procedures were performed based on the request of the referring physicians with no additional intervention.

All patients underwent post-stress and at rest protocol using three different methods of stress: Exercise (ETT), Dipyridamole infusion or Dobutamine infusion. During all these three protocols of stress, electrocardiographic monitoring was performed. If viability assessment was requested by the referring cardiologist, a dose of 111 MBq (3 mCi) Tl-201 was used for the stress study and a dose 37 MBq (1 mCi) Tl-201 for the rest study (stress re-injection redistribution protocol). For the remaining cases, a dose of 740 MBq (20 mCi) of ^{99m}Tc-sestamibi was used for the stress study and a dose of 740 MBq (20 mCi) ^{99m}Tc-sestamibi for the rest study, as parts of two-day standard protocol of MPI.[6] A commercial MIBI kit (AEOI, Tehran, Iran) was used and the labeling and quality control procedures were performed according to the manufacturer's instructions. Image acquisition was performed with a rotating, single head ADAC gamma camera. All data acquisitions (rest and stress for three different protocols of stress) employed low energy, high resolution parallel hole collimation with step and shoot mode, matrix size of $64 \times 64 \times 16$, and using a roving 38.0-cm^2 detector mask.

Two nuclear medicine physicians blinded to other clinical characteristics interpreted SPECT data considering the presence (abnormal scan) or absence (normal scan) of myocardial perfusion abnormality (including either ischemia or infarction) and final diagnosis was reached by consensus. Semiquantitative visual interpretation was performed with short-axis and vertical long-axis myocardial tomograms divided into 20 segments for each study.[7] These segments were assigned on six evenly spaced regions in the apical, midventricular, and basal slices of the short-axis views and two apical segments on the midventricular long-axis slice. A perfusion score between 0 to 4 was assigned to each segment (0 = normal uptake to 4 = absent uptake in the segment). A summed stress score (SSS) was obtained by adding the scores of 20 segments of stress images. SSS < 4 were considered normal; 4 to 8, mildly abnormal; 9 to 13, moderately abnormal; and > 13, severely abnormal.[7] As the semi-quantitative index, SSS was considered for the statistical analysis, as based on the previous reports, it is the most significant determinant of prognosis derived from MPI.[7]

Follow-up

Patients' follow-up was performed by telephone interview by a physician interviewer blinded to the patients' MPI results and also from the hospital records. The follow-up period was described as the total of all clinical information available after the MPI examination, including history taking, clinical examinations, invasive procedures, and outcome of admissions performed at a later date.

Events were defined as either cardiac death as described by relatives and recorded by death certificate or nonfatal myocardial infarction as notified by reporting the combination of symptoms, ECG, and enzyme changes and confirmed by hospital records.

Statistical analysis

Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's *t*-test or Mann-Whitney U test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA).

Results

The clinical characteristics of 510 patients who underwent MPI during the year 2005 are presented in Table 1. Of these, 377 patients (73.9%) had at least one major risk factor for CAD, the most common of which was hypertension (43.1%). Successful follow-up was achieved for 482 patients (follow-up rate, 94.5%). The mean follow-up interval was 434 ± 62 days. During the follow-up period, 14 out of 482 patients (2.9%) died from cardiac events. Also in 61 patients (12.7%), the clinical condition led to a cardiac intervention (PCI or CABGs).

Descriptive patient characteristics and scintigraphic variables in patients with or without events on follow-up are presented

Table 1
Demographic characteristics and follow-up data of the studied patients[a]

Baseline characteristics (n = 510)[b]	
Variable	Frequency
Male gender	265 (52.0%)
Age (year)	54.3 ± 12.3 Yr
Chest pain	
Typical	106 (20.8%)
Atypical	211 (41.4%)
Diabetes mellitus	136 (26.7%)
Dyslipidemia	218 (42.8%)
Hypertension	220 (43.1%)
Cigarette Smoking	52 (10.2%)
Previous CABGs	42 (8.2%)
Previous PCI	24 (4.7%)
Events during the Follow-up (n = 482)	
Summed Stress Score (SSS)	6.5 ± 2.2
Cardiac death	14 (2.9%)
Myocardial infarction	29 (6.0%)
Revascularization	
CABGs	10 (2.1%)
PCI	51 (10.6%)

CABGs: Coronary Artery Bypass Graft surgery; PCI: Percutaneous Coronary Intervention.
[a] Data are presented as mean ± SD or number (percentage).
[b] Based on the data obtained by interview at the time of myocardial perfusion imaging.

in Table 2. Those patients without cardiac events on follow-up (including cardiac death or myocardial infarction) were younger ($P < 0.05$) and with less severity of MPI abnormalities ($P < 0.05$). With respect to the extension and severity of scan abnormalities in event groups, severe MPI abnormalities (SSS > 13) was found in 42.9% of those with cardiac death, while in 17.2% of those with myocardial infarction. The rate of cardiac death had a direct relationship with the severity of scan abnormalities ($P = 0.004$), however, the same association was not found between the severity of MPI abnormality and the rate of myocardial infarction ($P = 0.551$) (Fig. 1).

Discussion

Our study showed that patients with normal to mildly abnormal MPI scans are at low risk for future cardiac death. As it was stated by previous reports, a normal or near normal MPI indicates a favorable prognosis, because many of the determinants of an unfavorable prognosis in CAD can be assessed by MPI.[8]

The rate of cardiac death increases significantly with severity of scan abnormalities. This figure is comparable with those reported in previous studies.[9–30] However, in our study, this association does not exist between the occurrence of myocardial infarction as an event and severity of MPI abnormalities. Our explanation is the low number of patients with MI in the follow-up, which decreases the power of our study to find a statistically significant relationship.

Recent studies have shown that MPI is a useful tool, especially in the patient population with low to intermediate probability of ischemic cardiac events. Also its high sensitivity in the detection of myocardial infarction has been confirmed. Moreover, it enables risk stratification and provides incremental and independent prognostic information regarding short to long term future cardiac adverse events.[9] Johansen et al. also showed that patients with normal perfusion imaging had only annual event rate of 1.6% and confirmed that in patients with known or suspected stable angina, MPI is a valuable risk stratifying tool.[8] Moreover, Elhendy et al. found that in patients with typical angina complaints, a normal MPI is indicative of an annual event rate of 1.5%, but MPI with perfusion abnormalities is indicative of an annual event rate of 4.5%.[10] In this line, Kontos et al. found that a positive MPI scan is the only predictor of myocardial infarction in a multivariate analysis and the most important independent predictor of myocardial infarction or revascularization.[11]

Also in our study, similar to other recent reports, summed stress score (SSS) was an important predictor for cardiac events.[4,15–17] It seems that integrating information about risk factors for CAD allows detailed risk stratification after intervention.[18] However, the role of other probable effective factors such as type of surgery and indices for the assessment of cardiac function should be evaluated in each population.

Our study also found significant relationships between cardiac events and other factors such as age and history of hypertension and diabetes mellitus. These associations have been commonly shown in other populations. In Matsuo et al. survey, diabetes mellitus, age and hypertension were independent predictors of all cardiac events.[12] Another study revealed that the elderly were at a higher risk, with an increased underlying disease and event burden that prevents identification of those at very low risk.[13] Furthermore in De Lorenzo et al. study, age, diabetes mellitus and shortness of breath as the presenting symptom were independent predictors of cardiac events.[14]

Table 2
Clinical and scintigraphic variables in patients with or without events on follow-up (n = 482).

Patients' characteristics	Cardiac events		No event (n = 439)
	Cardiac death (n = 14)	MI (n = 29)	
Male Gender	8 (57.1%)	22 (51.2%) 14 (48.3%)	228 (51.9%)
Age (Yr ± SD)[a]	68.9 ± 11.3 yr	63.0 ± 12.2 yr 60.1 ± 13.2 yr	53.5 ± 11.9 yr
Chest Pain	8 (57.1%)	30 (69.8%) 22 (75.9%)	270 (61.5%)
Summed Stress Score (SSS)[a,b]	9.1 ± 3.3	7.5 ± 2.8 6.7 ± 2.1	6.4 ± 2.1
History of Diabetes Mellitus[a,b]	10 (71.4%)	20 (46.5%) 10 (34.5%)	108 (24.6%)
History of Dyslipidemia[a]	6 (42.8%)	22 (51.2%) 16 (55.2%)	186 (42.3%)
History of Hypertension[a]	8 (57.1%)	28 (65.1%) 20 (68.9%)	180 (41.0%)
Cigarette smoking	1 (7.1%)	5 (11.6%) 4 (13.7%)	44 (10.0%)

[a] Statistically significant difference between cardiac event and no cardiac event groups ($P < 0.05$).
[b] Statistically significant difference between cardiac death and myocardial infarction ($P < 0.05$).

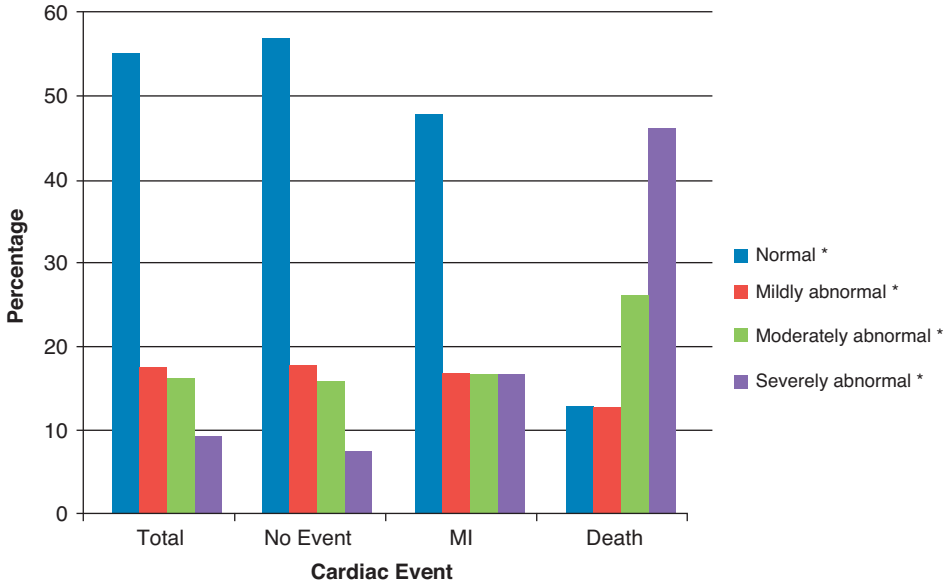

Figure 1. Association between MPI abnormalities and the rate of cardiac events on the follow-up. Although the rate of cardiac death was significantly related to severity of scan abnormalities ($P = 0.004$), however, the same association was not found between the severity of MPI abnormality and the rate of myocardial infarction ($P = 0.551$). *Summed stress scores < 4 were considered normal; 4 to 8, mildly abnormal; 9 to 13, moderately abnormal; and > 13, severely abnormal.

Study limitations

Current state of the art of myocardial perfusion SPECT imaging is gated SPECT acquisition. The lack of gated SPECT findings is the major limitation of our study. Although the number of patients in the subgroup of myocardial infarction during the follow-up was more than the subgroup of cardiac death, we found no statistical relationship between severity of scan abnormalities in these patients with higher baseline scan abnormalities, which seems to be in opposed of previous reports. It seems that the number of patients in this group (29) was too low to detect such an association and the power of the study was not high enough to unmask this relationship. Further studies in the larger number of patients are needed to clarify the issue.

Conclusion

MPI is a valuable tool for risk stratification and prediction of future fatal cardiac events in Asian population. The risk of cardiac death as a mid-term outcome of coronary artery disease increases significantly with severity of MPI abnormalities.

Conflicts of interest

The authors have no conflicts of interest to declare.

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