

## Prognostic value of normal exercise Tc-99m Sestamibi myocardial perfusion imaging in Karachi, Pakistan

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### Abstract

**Objective:** To ascertain the hard event rate in local population with normal myocardial perfusion.

**Methods:** The study, which was conducted from August 2006 to January 2007, included 300 patients with normal exercise myocardial perfusion scan (MPS). Patients were categorized according to their pre-test probabilities for CAD. Patients with low pre-test probability for CAD were 136 and ranked in group A, while group B constituted 164 patients who had intermediate to high pre-test probability.

**Results:** During a follow-up of mean duration of  $27 \pm 3$  months, an overall hard cardiac event rate of 1.02% was noted. However, a statistically non-significant difference between the survival rates of low and high pre-test probability groups was also observed.

**Conclusion:** The study demonstrated good prognosis for patients with normal exercise myocardial perfusion scan.

**Keywords:** Prognosis, Hard event, Survival, Myocardial perfusion scan (MPS) (JPMA 62: 351; 2012).

### Introduction

Stress myocardial perfusion imaging is one of the most commonly used non-invasive tests for the detection of Coronary Artery Disease (CAD). It has been proven to be cost-effective in the selection of patients for angiography and revascularisation, especially when used in patients with intermediate (CAD) risk.<sup>1</sup>

It also provides important prognostic information in patients with known or suspected CAD.<sup>2</sup> In a pooled analysis of 20963 patients from 16 published studies in the literature with a follow-up of slightly more than two years, the hard

event rate i.e. cardiac death and non-fatal myocardial infarction (MI) was 0.7% per year.<sup>3</sup> Even patients with positive exercise tolerance test for ischaemia or angiographically documented CAD but normal myocardial perfusion scan (MPS) have been shown to be at low risk for future cardiac events.<sup>4</sup>

It is a common belief that South Asians are more prone to developing CAD<sup>5</sup> and some studies also substantiated it by proving that there is increased prevalence of risk factors of CAD among Pakistanis.<sup>6,7</sup> Therefore, this study was conducted with the aim of ascertaining whether the

same hard event rate exists in patients hailing from South Asia with normal myocardial perfusion.

### Patients and Methods

This cross sectional study was conducted at the Atomic Energy Medical Centre, Jinnah Postgraduate Medical Centre, Karachi. All suspected CAD patients who were referred between August 2006 and January 2007 for MPS and whose stress perfusion scans were considered normal were included in the study. Patients with prior myocardial infarction or with pathological Q waves in their ECGs, history of unstable angina, severe arrhythmia, idiopathic cardiomyopathy or prior history of revascularisation were excluded from the study.

All the patients gave informed consent before the test. The Institute's Ethical Committee approved the protocol. Clinical history was acquired and cardiac risk factors were assessed before nuclear testing.

Patients were categorised into low, intermediate and high risk groups for CAD utilising the clinical score derived by Morise AP<sup>8</sup> (Table-1). Patients with low pre-test probability for CAD were 136 and ranked in group A, while group B constituted those 164 patients who had intermediate to high pre-test probability.

All patients underwent two Tc-99m MIBI (Methoxy-Isobutyl-Isonitrile) SPECT (Single Photon Emission Computed Tomography) studies (1 day protocol); one with exercise called as Stress MIBI study and one under resting conditions called Rest MIBI study. Besides, 10 & 30 mCi[99m]Tc-MIBI were injected intravenously and flushed with normal saline for stress and rest studies respectively. Patients were asked to have a light fatty meal shortly after injection and images were acquired 30-45 minutes later.

All patients underwent symptom-limited Exercise Tolerance Test (ETT) using the Bruce protocol according to standard guidelines.<sup>9</sup>

At peak exercise (at least 85% of age-predicted heart rate or upon development of symptoms), Tc-99m MIBI was injected as a bolus into an intravenous line and flushed with 5 ml of NaCl 0.9% solution 1 minute before the end of the exercise.

SPECT acquisition was performed using a rotating large field of view gamma camera equipped with low-energy general-purpose parallel hole collimator interfaced to a dedicated computer system. Total 32 frames 30 seconds each were acquired in continuous acquisition mode over 180 degrees, anteriorly in a circular arc, with a starting angle of 45 degrees right anterior oblique (RAO) position to the 135 degrees left posterior oblique position. A 15% symmetrical energy window centered at 140 keV was employed.

For each MPS, short axis, vertical long axis and

horizontal long axis slices were defined. The interpretation of scan was performed by visual analysis. Stress and rest tomographic views were reviewed side by side by two experienced observers who were unaware of the patients' clinical and angiographic data. In cases of disagreement, a third reader was called in for interpretation.

All selected patients were prospectively followed up during August 2006 and June 2009 for a mean period of  $27 \pm 3$  months for the study. Data were collected biannually by contacting the patients or their immediate relatives on telephone. In cases of hospitalization, medical record was reviewed subsequently. The end points were death from any cause or any hard cardiac event (cardiac death and non-fatal MI, defined by cardiac enzyme levels and ECG changes). Death was considered cardiac if it was caused by acute MI, significant arrhythmias and heart failure.

Continuous variable like age was presented as the mean standard deviation. For survival curve Kaplan-Meier curve was drawn using SPSS version 10. Comparison between the two groups was done by Log-Rank Test. Statistical significance was set at  $p < 0.05$ .

### Results

Clinical characteristics and the prevalence of CAD risk factors such as hypertension and diabetes mellitus were noted (Table-2). The mean age was  $50.16 \pm 10.47$  years. There were 165 (55%) men. All patients underwent exercise stress test and achieved optimum heart rate ( $\geq 85\%$  of target heart rate). Only 44% of patients had an ischaemic response to exercise.

Out of 300 patients, 5 were lost during the follow-up process; one due to non-cardiac death and the other four could not be followed up. Two of them belonged to group A while

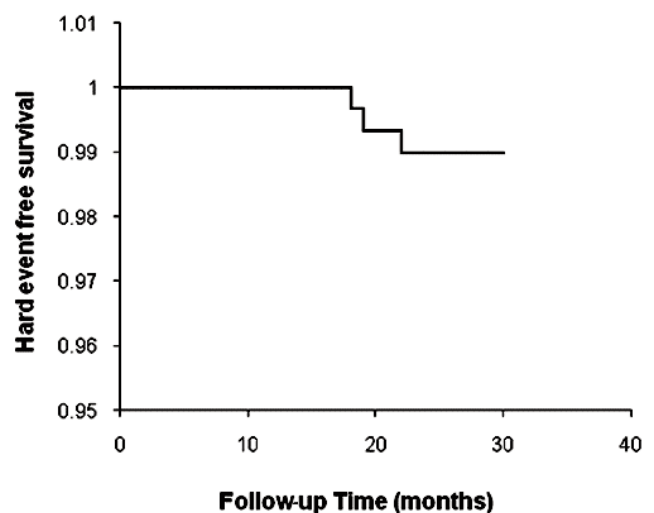


Figure-1: Kaplan-Meier survival curve showing overall survival of 98.98% over follow-up of mean duration of 27 months in patients with normal myocardial perfusion scan (MPS).

**Table-1: Scoring Method.**

Age	Men	Women	Points
	<40 years	<50 years	3
	40-54 years	50-64 years	6
	≥ 55 years	≥ 65 years	9
Oestrogen Status			Positive = -3
Women only			Negative = +3
Male			0
Symptoms			Typical angina = 5
			Atypical angina = 3
			Non angina = 1
Risk factors	Diabetes		2
	Hypertension		1
	Smoking		1
	Hyperlipidaemia		1
	Family history		1
	Obesity, BMI >27		1
<b>Low Probability:</b>	<b>Intermediate Probability:</b>	<b>High Probability:</b>	
0-8 points	9-15 points	16-24 points	

BMI: Body Mass Index.

**Table-2: General characteristics of patients.**

General Clinical Data	Group A (n=136)	Group B (n=164)
Mean age in years	45.99 ± 8.74	54.06 ± 10.39
Male Gender	51 (38%)	114 (70%)
DM	22 (16%)	98 (60%)
ECG changes	56 (41%)	75 (46%)
Hypertension	90 (66%)	138 (84%)
Smoking	27 (20%)	60 (37%)
Hyperlipidaemia	48 (35%)	29 (18%)
Family History	24 (18%)	60 (37%)
Chest pain	45 (33%)	51 (31%)
Obesity	30 (22%)	18 (11%)

SD, Standard deviation; DM, Diabetes Mellitus; ECG, Electrocardiogram.

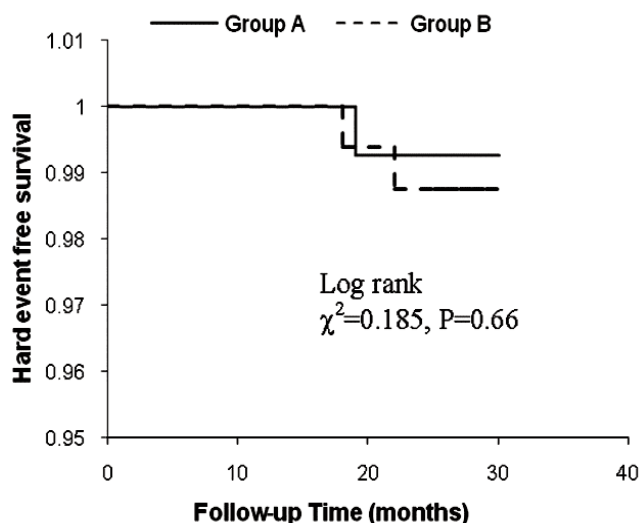


Figure-2: Kaplan-Meier survival curve, showing survival of 98.76% in patients with high pre-test probability and 99.26% in low pre-test probability over follow-up of mean duration of 27 months after normal MPS.

the rest were from group B. None of the patients underwent revascularization, although 6 of them required hospitalisation for 1-2 days for the evaluation of their chest pain.

There was only one hard event (non-fatal MI) reported in group A, while two such cases were noted in group B. The overall annual hard cardiac event rate was found to be quite low i.e. 1.02% (Figure-1). However, when calculated only in group A, it was estimated to be 0.74% and group B showed a hard event rate of 1.24% (Figure-2). Statistically, no significant difference was noted between the survival curves of the groups ( $\chi^2=0.185$ ,  $P=0.66$ ).

## Discussion

Various studies have already been published showing < 1% hard event rate in patients with normal MPS when followed for short term.<sup>10</sup> But keeping in mind the fact that cardiac event rate among countries varies according to ethnicities,<sup>11</sup> and, indeed, the increased prevalence of CAD risk factors among Pakistanis and insufficient data related to the local population, the study was planned to determine whether a similar survival rate exists in Pakistani patients with normal exercise MPS.

The study evaluated the prognostic significance of normal myocardial perfusion scan by 99mTc-MIBI in 300 patients which were divided into two groups according to their pre-test CAD probabilities. The yearly cardiac hard event for the total group was low i.e. 1.02%. Similar findings were related by Fattah et al,<sup>12</sup> which showed an annual event rate of 1.1% (two cardiac deaths and one non-fatal MI) in patients with normal 201-Tl myocardial SPECT when followed up for 32 months. They investigated 97 patients, of whom 21 underwent revascularization.<sup>12</sup> Comparable results are also seen by Zaman et al in Karachi. The event rate was 0.6% in a study population of 267 patients when followed up for 15±3 months.<sup>13</sup>

Most of the studies proved good prognostic value of normal MPS independent of the clinical factors of the patients. Berman et al<sup>14</sup> also demonstrated that the cardiac event rate for patients with normal scans was low for all levels of pre-test likelihood of CAD after the acquisition of exercise ECG stress test results.<sup>14</sup> In our study, although relatively increased hard event rate was noted in the high-risk group as compared to the low-risk group, statistically no significant difference was observed between the two supporting the concept that, even in a patient with a high pre-test probability, a normal MPS reduces the risk of future cardiac events.

However, Poornima et al<sup>15</sup> in their study showed that patients with greater clinical score have higher hard event rate as compared to those who had a low clinical score, although both had normal MPS. However, the authors did not provide

information regarding the significance of difference between the groups.<sup>15</sup>

Another study published by Yosihro Imamura et al<sup>16</sup> provided statistically significant difference when comparison was done between the event rates of low vs intermediate and low vs high-risk CAD groups ( $p < 0.001$ ).

The outcome of our study has significant worth not only for the prediction of future cardiac events, but also for planning treatment strategies. Patients with normal cardiac scans can be spared from further invasive procedures until their clinical status changes. This will result in considerable cost-savings and patient comfort.

Though the study calculated the pre-test likelihood of CAD, it is believed that it would have been better if some exercise variables were also included for the risk stratification of CAD. Another possible limitation was the non-availability of gated studies. Furthermore, all images were assessed by visual/qualitative interpretation. With more patients followed up over a longer period of time, the results would have more impact.

### Conclusion

Despite its limitations, the study demonstrated good prognosis for patients with normal exercise MPS. Although no significant difference was observed between the survival rate of low and high pre-test probability groups, further studies with longer duration are recommended to establish the independent prognostic value of normal MPS irrespective of pre-test probability.

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