Research Article

The Effect of Long Term Smoking as an Independent Coronary Risk Factor on Myocardial Perfusion Detected by Thallium 201 or Tc99m Sestamibi Spect Study

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Abstract

Objective: The aim of this work was to assess the effect of smoking as an independent coronary risk factor on Myocardial Perfusion detected by Thallium 201 or Tc99m Sesta MIBI SPECT study.

Methods: This study included 200 patients, 100 who are smokers only (group A) without any cardiac risks and the other 100 (group B) were nonsmokers, but with single cardiac risk factor as hypertension or diabetes. Each was subjected to Dipyridamole (smokers 53, 47) or exercise (nonsmokers 51, 49) Thallium-201 or Tc99m SestaMIBI SPECT protocol.

Results: Comparing smokers versus nonsmokers who have another one risk factor, smokers had : Lower age with ischemic heart disease 55 years versus 60 years; Higher heart rate during peak stress; higher blood pressure during peak stress; More incidence of chest pain during stress test; had the same degree of ischemic perfusion defect, but higher incidence of persistent LV dilatation (43% versus 28%), higher incidence of severe perfusion defects (68% versus 53%) and statistically significant higher incidence of scar tissue (52% versus 30%).

Conclusion: Smoking is an independent risk factor equal to hypertension and diabetes but smokers has higher incidence of severe perfusion defects and scar.

Abbreviations: SPECT: Single-Photon Emission Computed Tomography; MPI: Myocardial Perfusion Imaging; CAD: Coronary Artery Disease; MAP: Mean Arterial Pressure

Introduction

Decision-making using SPECT-MPI is based on its proven prognostic efficacy. Principally, a normal SPECT-MPI study establishes patients who are at low risk of subsequent adverse clinical events; clinical risk increases in exponential relationship to the magnitude of inducible myocardial ischemia. In particular, the presence of hypertension, smoking, and diabetes were all significant predictors of long-term risk. Annual all-cause mortality rate was 0.2% among patients with none of these three risk factors, 0.6% among those with one of these risk factors, 1.3% with two of these risk factors, and 1.7% for those with all three of these risk factors [1-4]. Smoking is a major recognized risk factor for cardiovascular disease, being associated with an increase in vascular morbidity such as myocardial infarction and sudden death [5-9]. Clinical studies have demonstrated that smoking causes endothelial dysfunction in the systemic circulation, but the mechanisms by which this occurs have not been fully elucidated, although substantial evidence is accumulating that suggests increased superoxide anion generation may play a critical role [10]. The value of thallium technique in elucidating risk factors influence on myocardial ischemia is studied and proved [11-15].

The aim of this work is to assess the effect of smoking as an independent coronary risk factor on Myocardial Perfusion detected by Thallium 201 or Tc99m SestaMIBI SPECT study.

Patients

This study included 200 patients, 100 patients who are smokers only without any cardiac risks and the other 100 patients are nonsmokers, with single cardiac risk factor. All these patients undergone myocardial perfusion scintigraphy SPECT study associated with either exercise stress test or dipyridamole stress in the data base Nuclear Cardiology Lab. Cardiology Department in Alexandria Main University Hospital as well as the prospective consecutive patients in the period of 6 months from March 2015. Consent was taken from all patients to participate in the study.

The following patients were excluded:

- Patients with contraindications to cardiac stress test
- Patients with history of severe valvular heart disease
- Patients with severe heart failure (EF below 40%)
- Ex-Smokers
- Pregnancy
- Patients who did not give their consent

We did not count how many patients were excluded. After including the 200 patients, any new patients were not added.

Written consent to include in a study was obtained from each patient; and the ethical committee of the Faculty of Medicine approved the study protocol.

Methods

Indication for inclusion in thallium stress test: all patients had complaints suggestive of coronary heart disease as chest pain, some ECG changes, and positive family history and asked to check their hearts.

Diabetic patients: All were type two, defined as diabetic if A1c level is 6.5 or more, fasting blood sugar is >126 mg/dl twice or post prandial level >200 twice or one reading >250 mg/dl or are taking antidiabetic medicines. All diabetic patients were controlled or not severely uncontrolled.

Hypertension was defined if patient is taking antihypertensive medicines or reading is >150/90 twice in two occasions and following the standard roles of measuring blood pressure.

All patients were subjected to:

History

- Personal History: name, age and gender.
- Present History: especially about chest pain (onset, predisposing factors, duration, and treatment). History of dyslipidaemia.
- Past History:
- -Diabetes Mellitus, Hypertension (duration and control).
- -Myocardial infarction and prior revascularization.
- Family History: of coronary artery disease, Diabetes Mellitus, Hypertension and dyslipidemia.
- Social History: of smoking (smoking index: number of cigarettes smoked per day and the duration of smoking) and alcohol intake.
- Drug History: especially Digitalis, Beta Blocking Agents, Calcium Channel Blockers, Antiarrhythmic drugs, ACEIs, ARBs, Aspirin.

Clinical examination

Clinical examination including heart rate, blood pressure, weight and height; chest examination to exclude bronchospasm in case of need to use Dipyridamole.

Standard 12 lead Electrocardiogram (ECG)

Myocardial perfusion SPECT study

Stress, rest Dipyridamole or exercise Thallium-201 or Tc99m SestaMIBI SPECT protocol to study myocardial perfusion [10].

Dipyridamole protocol

- Patients were instructed to avoid xanthine medication and caffeinated beverages 12 h before the test.
- Intravenous infusion of 0.56 mg/kg body weight/min for 4 min
- Radioactive agent will be injected IV at the end of 2 min post completion of Dipyridamole

- Intravenous aminophylline 100-200 mg will be given 3-4 min after injection of Thallium if there is severe chest pain or bronchospasm after 2 trials of using sublingual nitrates

The following parameters were recorded during Dipyridamole stress of a multivariate analysis in relation to the myocardial perfusion data:

- Typical angina chest pain: (onset and duration during Dipyridamole stress test).
- Resting heart rate and the heart rate response to Dipyridamole infusion.
- Resting blood pressure and blood pressure response to Dipyridamole infusion.
- ECG changes: ST-segment depression, T-wave inversion, any kind of arrhythmia.

Exercise stress test protocol

Exercise with standard Bruce Tread mill exercise protocol (beta blockers and calcium channel blockers stopped 48 h before the test). Exercise was stopped if positive changes appeared or patient got limiting symptoms.

The following parameters were recorded for multivariate analysis with the myocardial perfusion data:

- Typical angina pain: onset and duration during exercise stress test
- ST changes: depression >2 mm horizontal or down sloping or up sloping ST segment >1.5 mm at 80 msec or more after J point in at least 3 consecutive beats in 2 or more leads during or after exercise.
- Changes in heart rate
- Changes in blood pressure
- Hypotensive response: systolic B.P<85 mmHg
- Hypertensive response: systolic B.P>220 mmHg and/or diastolic B.P>120 mmHg.
- Functional capacity (METs)
- Any kind of arrhythmia.

The myocardial perfusion study

Every Patient received 3 to 3.5 mCi Thallium-201 at peak stress, and myocardial perfusion imaging will be initiated within 10 min afterward. The delayed resting study with Thallium was done by reinjection of 1 mCi after 3-4 h; and imaging after 20 min. For Tc99 m Sesta MIBI the 2-day protocol was used. Stress imaging after injection of 20 mCi Tc99 m Sesta MIBI and peak stress imaging after an hour after a fatty meal. The resting study was in the second day after injection of 20 mCi Tc99 m Sesta MIBI and imaging after an hour during which the patient should take a fatty meal. Imaging was done by Siemens, double head Symbia E Gama camera in supine position from right anterior oblique to left posterior oblique. The myocardial perfusion uptake was studied in 17 segments model, using 4 point scale [10].

0: Normal.

1: Mild reduction of the uptake.

2: Moderate reduction of the uptake.

3: Severe reduction of the uptake.

4: Absence of detectable tracer uptake.

Summed stress and rest scores were obtained by adding the scores of 17 myocardial segments on the basis of three short-axis slices and a representative long-axis slice to depict the apex. The sum of the differences between these 2 scores defined the summed difference score. These indexes were converted to a percent myocardium with abnormal stress, ischemic, or fixed defects by dividing the summed scores by 68; the maximum potential score (4 points X 17 segments), and multiplying by 100. Normal scans and mildly and moderately to severely abnormal scans were defined as percent myocardium abnormal <5%, 5% to 10%, and >10% myocardium [14].

SPECT study was not ECG-gated; attenuation correction was applied. Imaging interpretation was visual as well as by quantitative software.

Dipyridamole was the stress method in 53% and 51% in smokers group, and exercise stress was in 47% and 49% in nonsmokers group (insignificant difference).

The METS (metabolic equivalent) achieved by exercise ECG were in total not different in the two groups. Only typical angina was counted as sign, not just chest discomfort. No attenuation correction was applied.

Statistical analysis

Data were entered in the computer and analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. The used tests were: Chi-square test: For categorical variables, to compare between different groups. Fisher's Exact or Monte Carlo correction: Correction for chi-square when more than 20% of the cells have expected count less than 5. Student t-test: For normally quantitative variables, to compare between two studied groups. Paired t-test: For normally quantitative variables, to compare between two periods. Mann Whitney test: For abnormally quantitative variables, to compare between two studied groups. Wilcoxon signed ranks test: For abnormally quantitative variables, to compare between two periods quantitative variables.

Results

Baseline demographic data are in Table 1.

Parameters	Group A Smokers (Number mean ± SD)	Group B Non-Smokers (Number mean ± SD)	P value
Age	55.45	60.49	0
Male/Female	100	53	0
Heart rate at rest	76.5 ± 13	77 ± 13.7	0.865
Heart rate at peak exercise	111.5 ± 30.8	94 ± 30.3	0
Blood pressure systolic at rest	127 ± 15.9	141 ± 20.1	0
Blood pressure diastolic at rest	81 ± 9.1	85 ± 10.2	0.003
Blood pressure systolic at peak	148 ± 22	139 ± 17.8	0.007
Blood pressure diastolic at peak	87 ± 11.8	85.9 ± 8.5	0.102

Table 1: Comparison between the two groups as regards some parameters

Patient's risk factor has been demonstrated in Table 2.

Risk Factors	Group (A) Smokers (n=100)		Group (B) Non-Smokers (n=100)	
	No.	%	No.	%
DM	0	0	85	85
HTN	0	0	57	57
Smoking	100	100	0	0
Duration years	32.4 ± 8.7			
No. of pack/day	0.89 ± 0.27			

Table 2: Comparison between the two groups as regard the risk factors

There was no significant difference between percent of positive family history and dyslipidemia between the two groups.

Patient's chest pain and ECG changes during stress are in Table 3.

	Group (A) Smokers (n=100)		Group (B) Non-Smokers (n=100)		P Value
	No.	%	No.	%	
ECG changes No	79	79	76	76	
ECG changes Yes	21	21	24	24	0.735
Total	100	100	100	100	
Chest pain No	52	52	86	86	
Chest pain Yes	48	48	14	14	0

Table 3: Comparison between the two groups as regard ECG changes and the chest pain

Patient's myocardial perfusion defect is in Table 4. There was statistically significant difference between the studied groups as regard to LCX defect where P=0.021.

Myocardial defect	Group (A) (n=100)		Group (B) (n=100)		P Value
	No	%	No	%	
LAD	85	85	88	88	0.68
RCA	51	51	47	47	0.671
LCX	32	32	49	49	0.021

Table 4: Comparison between the two groups as regard the myocardial defect

Patient's Left ventricle in Group (A) 31 (31%) were normal, 26 (26%) with transient LV dilatation and 43 (43%) with persistent dilatation while in Group (B) showed that 45 (45%) were normal, 27 (27%) with transient dilatation and 28 (28%) with persistent dilatation. (Table 5). Assessment of dilatation was done visually. Measurement of ejection fraction after stress was not done.

Left ventricle	Group (A) (n=100)		Group (B) (n=100)		P Value
	No	%	No	%	
Normal	31	31	45	45	
Transient dilatation	26	26	27	27	
Persistent dilatation	43	43	28	28	
Total	100	100	100	100	0.056

Table 5: Comparison between the two groups as regard the left ventricle

Patient's degree of myocardial perfusion defect in (Table 6).

Ischemia	Group (A) (n=100)		Group (B) (n=100)		P Value
	No	%	No	%	
No	4	4	2	2	
Mild	12	12	25	25	
Moderate	16	16	20	20	
Severe	68	68	53	53	
Total	100	100	100	100	0.057

Table 6: Comparison between the two groups as regard the ischemia

Patient's Scar in Group (A) 48 (48%) had no scar and 52 (52%) had scar while in Group (B) showed that 70 (70%) had no scar and 30 (30%) had scar (P=0.002) (Table 7 and Figure 1).
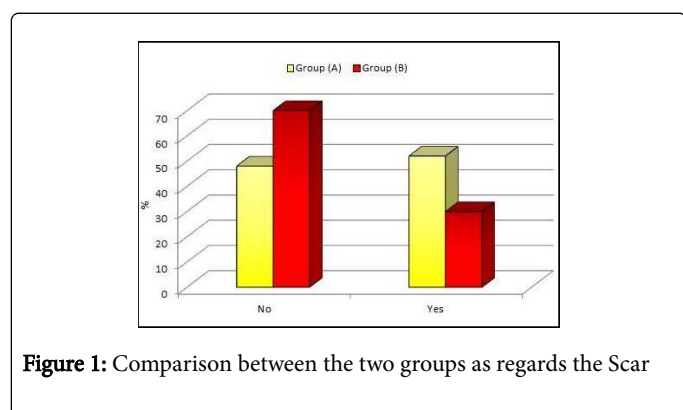

Figure 1: Comparison between the two groups as regards the Scar

There was positive but not significant correlation between smoking (duration and No. of packs/day) and ischemia while there was positive but not significant correlation between smoking (duration and No. of packs/day) and scar. Correlation of resting ECG with scar in thallium was not done. Results of ECG changes with stress exercise or pharmacologic were recoded positive or negative, we did not record

severity of ECG changes and did not compare it in the two stress modalities.

		Smoking	
		Duration	No. of packs/day
Ischemia	r	0.067	0.015
	P	0.507	0.886
Scar	r	-0.052	-0.012
	P	0.605	0.908

Table 7: Correlation between smoking duration and the severity of ischemia or scar

Patient's coronary artery territory affection in (Table 8), coronary artery territories were assessed according to standard protocols [10].

Coronary Artery Territory Affection	Group (A) (n=100)		Group (B) (n=100)		P Value
	No	%	No	%	
1 Vessel affection	47	47	43	43	
2 Vessel affection	38	38	30	30	
3 Vessel affection	15	15	27	27	0.103
Total	100	100	100	100	

Table 8: Comparison between the two groups regarded to coronary artery territory affection

Discussion

In our this study, the myocardial perfusion defect in Group (A) (4%) had no ischemia, (12%) had mild ischemia, (16%) had moderate ischemia and (68%) had severe ischemia while in Group (B) showed that (2%) had no ischemia, (25%) had mild ischemia, (20%) had moderate ischemia and (53%) had severe ischemia; P=0.057. Thus smoking alone as a single risk factor can cause ischemia equal to that due to the other risk factors, but with tendency to more incidence of severe ischemia. Also scar was more in smokers (48% vs. 30%; p<0.002).

In a study [9], to evaluate the effect of tobacco smoking on the risk of nonfatal acute myocardial infarction in young adults (≤ 45 years), it was found that the prevalence of current smoking was 80.8% in male cases and 53.8% in male controls (OR=3.63, 95% CI: 2.50, 5.27) and 59.5% of female cases were smokers compared with 35.8% of controls (OR=2.64, 95% CI: 1.39, 5.02). No interaction was found between current smoking and gender on myocardial infarction risk (P=0.401). A dose-effect response was present, the odds favoring myocardial infarction reaching an eight-fold increase for those who smoked >25 cigarettes/day compared with never smokers. The risk estimate for former smokers was similar to never smokers. Thus tobacco smoking is an important independent risk factor for acute myocardial infarction in young adults, with similar strength of association for both genders.

In the study by Papathanasiou et al., it was found that smokers had significantly higher resting HR values than non-smokers [7]. The

actual maximum HR achieved (HRmax) was significantly lower for both female smokers (191.0 bpm vs. 198.0 bpm) and male smokers (193.2 bpm vs. 199.3 bpm), compared to non-smokers. In our study there were no female smokers.

In the study by Linneberg et al., the data on 141,317 participants (62,666 never, 40,669 former, 37,982 current smokers) from 23 population-based studies were included in observational and Mendelian randomization meta-analyses of the associations of smoking status and smoking heaviness with systolic and diastolic blood pressure, hypertension, and resting heart rate [8]. In observational analyses among current smokers, 1 cigarette/day higher level of smoking heaviness was associated with higher (0.21 bpm; 95% confidence interval 0.19; 0.24) resting heart rate and slightly higher diastolic blood pressure. These findings suggest that part of the cardiovascular risk of smoking may operate through increasing resting heart rate.

Lindsay et al. reported that patients experienced almost universal improvement with the CABG operation [4]. However, persistent smoking completely removed the prognostic benefits of CABG by accelerating late mortality which was higher than previously reported. They stated that higher indices of ischaemia in smokers were suggested by symptoms and confirmed by perfusion scans.

Conclusion

Comparing smokers versus nonsmokers who have another one risk factor, smokers had:

- Lower age with ischemic heart disease 55 years versus 60 years.
- Higher heart rate during peak stress.
- Lower resting blood pressure.
- Higher blood pressure during peak stress.
- More incidence of chest pain during stress test.

Had the same degree of ischemic perfusion defect as well as the effect of ischemia on LV size, but higher incidence of persistent LV dilatation (43% vs. 28%), higher incidence of severe perfusion defects (68% vs. 53%) and statistically significant higher incidence of scar tissue (52% vs. 30%). Smoking is a major risk factor for cardiac insults, leading to more scar, more ischemia and more LV dilatation.

Recommendation

Future studies should include current smokers to be compared with patients after smoking cessation by at least five years; also to follow up the severity of ischemia in smokers after smoking cessation. Public awareness campaigns to explain the hazards of smoking on coronary artery disease should be encouraged in all types of media.

Limitations of the study

We stressed on risk factors as smoking, hypertension, and diabetes; other risk factors may influence results as family history, hypercholesterolemia, and gender. Smokers group were all males. Nevertheless the difference of these factors in the two groups will not obviate the conclusions.

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