Can technetium-99m Sestamibi SPECT Predict the Presence of Chronic Total Occlusion in Patients with Coronary Artery disease and No Evidence of Previous Myocardial Infarction

Thesis

Submitted in partial fulfillment for MD Degree of Cardiology

By **Gehan Hassan Maghrabi Abd Allah** MBBCh. MSc.

Under Supervision of

Prof. Dr. Mohamed Mamdouh Mostafa El Achry

Professor of Cardiology Faculty of Medicine-Ain Shams University

Prof. Dr. Khaled Abd El-Latif Farouk El Menyawi

Professor of Cardiology Faculty of Medicine-Ain Shams University

Assist. Prof. Dr. Salah El-Din Hamdy Demerdash

Assistant Professor of Cardiology Faculty of Medicine-Ain Shams University

Assist. Prof. Dr. Hussein Saad Hussein shaalan

Assistant Professor of Cardiology Faculty of Medicine-Ain Shams University

هل باستطاعة المسح الذرى بواسطة مادة التكنشيوم ٩٩ التنبؤ بالإنسداد الكلى فى مرضى الشرايين التاجية للقلب بدون احتشاء ظاهر بعضلة القلب

رسالة مقدمة من الطبيبة / جيهان حسان مغربى عبد الله تؤطئة للحصول على درجة الدكتوراه في أمراض القلب و الأوعية الدموية جامعة عين شمس

تحت إشراف الأستاذ الدكتور / محمد ممدوح مصطفى العشرى أستاذ أمراض القلب و الأوعية الدموية كلية الطب – جامعة عين شمس

الأستاذ الدكتور / خالد عبد اللطيف فاروق المنياوى أستاذ أمراض القلب و الأوعية الدموية كلية الطب – جامعة عين شمس

الأستاذ الدكتور / صلاح الدين حمدى دمرداش أستاذ مساعد أمراض القلب و الأوعية الدموية كلية الطب – جامعة عين شمس

الأستاذ الدكتور / حسين سعد حسين شعلان أستاذ مساعد أمراض القلب و الأوعية الدموية كلية الطب – جامعة عين شمس

كلية الطب – جامعة عين شمس ٢٠٠٨

ACKNOWLEDGEMENT

I wish to express my deepest gratitude to *Prof. Dr. Mamdouh El Ashry*, Professor of Cardiology, Cardiology Department, Faculty of Medicine, Ain Shams University, for his unlimited support, guidance and expertise in the preparation of this work.

I am also in deeded to *Prof. Dr. Khaled El Menyawi*, Cardiology Department, Faculty of Medicine, Ain Shams University for his continuous assistance and his precious remarks.

Special acknowledgement also to *Ass. Prof. Dr. Salah Eldin Demerdash*, Cardiology Department, Ain Shams University for his unlimited support, continuos assistance, his keen supervision, kind guidance and precious advice.

Many thanks to *Ass. Prof. Dr. Hussein Shalan*, Cardiology Department, Ain Shams University for his kind guidance and supervision.

Very special thanks to all the members of Nuclear cardiology especially *Mr. Khaled El Banna* for their great help and cooperation.

Also my thanks to all members of the *Cath. Lab.* for their help. I wish all of them all the best.

CONTENTS

	Pag
	е
Acknowledgement	
List of contents	
List of tables	
List of figures	
Introduction	1
Aim of the work	3
Review of literature	4
Pathophysiology of myocardial ischemia	4
Diseases of the coronary arteries-causes, pathology and	
prevention	6
Chronic total occlusion in ischemic patients	13
Pathophysiology of chronic total occlusion	19
Coronary collaterals	20
Consequence of coronary occlusion and severe ischemia.	28
Myocardial viability	31
Non invasive tests in diagnosing coronary artery disease	35
Invasive methods in diagnosing coronary artery disease	47
Nuclear imaging	50
Technetium-99m labeled isonitriles	59
Physics of Tc-99m sestamibi	61
Clinical applications for use of technetium-99m sestamibi	73
Patients and Methods	82
Results	91

	Pag
	е
Discussion	128
Summary	144
Conclusion and Recommendations	147
References	149
Arabic summary	

LIST OF TABLES

Γable		Page
1	Relation between total chronic occlusion of ≥ 1 coronary arteries and the number of risk factors	92
2	Chest pain, the resting, exercise ECG parameters and echocardiographic findings in the studied patients.	93
3	Relation between occlusion of coronary arteries and total coronary artery status	101
4	LAD artery status by angiography and Tc-99m sestamibi SPECT	104
5	LCx artery status by angiography and Tc-99m sestamibi SPECT	107
6	RCA artery status by angiography and Tc-99m sestamibi SPECT	110
7	Correlation between coronary angiography, technetium 99-m SPECT and grade of collaterals (LAD)	
		114
8	Correlation between coronary angiography, technetium 99-m SPECT and grade of collaterals (LCx)	
		117

Table		Page
9	Correlation between coronary angiography, technetium 99-m SPECT and grade of collaterals	
	(RCA)	120
10	Screening power test of Tc-99m sestamibi SPECT for the detection of occlusion of coronary vessels using	
	angiography as a golden standard	122

LIST OF FIGURES

Figure		Page
1	The anatomy of the coronary arteries.	7
2	A diagrammatic representation of an atheromatous plaque showing outer cap containing collagen and smooth muscle cells, and inner core showing foam cells and extracellular cholesterol crystals. (with permission from Thompson G.R. (1989) A Handbook of Hyperlipidaemia. Current Science).	10
3	Microscopic CT images of a CTO. Left, The vasculature is filled with contrast in this 3-dimensional image of a chronic coronary occlusion. Bridging capillaries are readily seen connecting the adventitia with the interior of this lesion. The diffuse white areas are calcification. Right, Sequential sagittal sections of this lesion, showing the complete	
4	occlusion, bridging channels, and calcification. Top, Anatomy of the heart as projected on planar views. Bottom, Coronary artery territories on three planar views. The shaded area indicates the facing myocardium overlying the left ventricular cavity. (From Wackers FJTh: Artifacts in planner and SPECT myocardial perfusion imaging. Am. J. Card.	18 71
	Imaging 6:42, 1992).	

figure		Page
5	Left ventricular anatomy and coronary artery territories	
	on single-photon emission computed tomographic slices	
	taken from a 17-segment model. (Modified from Port	
	SC (ed): Imaging Guidelines for Nuclear Cardiology	
	Procedures, (Part 2. J. Nucl. Cardiol. 6: 469, 1999).	72
6	Schematic presentation of segmental analysis of	
	technetium -99 m sestamibi. (J.Nucl. Cardiology 1995;	88
	2: 101).	
7	Relation between coronary artery occlusion and chest	
	pain.	94
O	Deletion between consumer entering and	
8	Relation between coronary artery occlusion and	95
	resting ECG	93
9	Relation between coronary artery occlusion and	
	exercise ECG.	96
10	Relation between coronary artery occlusion and	
	ЕСНО	97
11	Total coronary artery status by angiography and Tc-99m	
11	sestamibi SPECT.	102
		102
12	LAD artery status by angiography and Tc-99m	
	sestamibi SPECT.	105

figure		Page
13	LCx artery status by angiography and Tc-99m sestamibi SPECT	108
14	RCA artery status by angiography and Tc-99m sestamibi SPECT.	111
15	Screening power of Tc-99m sestamibi SECT to detect total coronary artery occlusion.	123
16	A normal Tc-99m sestamibi myocardial perfusion SPECT	124
17	Resting ECG showing inverted T wave in LII, III, aVF, V_5 , V_6 (Patient no 30).	125
18	Tc-99m sestamibi myocardial perfusion SPECT study showing a partially reversible perfusion defect involving the inferolateral and lateral regions (Territary of the LCx), another reversible perfusion defect is seen involving the anterolateral, anterior and apical regions (Territory of the LAD) (Patient no. 30).	126
19	Left coronary angiogram showing totally occluded LCx (Patient no: 30)	127

LIST OF ABBREVIATION

¹⁸F-FDG : ¹⁸flouorine fluor deisxy glucose.

^{99m}Tc : Technetium 99m

ATP : Adenosine triphosphate

CAD : Coronary artery disease

CCU : Cardiac care unit

CK : Creatinine kinase

CPI : Carboxyisopropyl isonitrile

CT : Computed tomography

CTO : Chronic total occlusion

DM : Diabetes mellitus

ECG : Electrocardiography

Echo : Echocardiography

FGF : Fibroplastic growth factor tomography

IAVs : Interconnecting anastomotic vessels

LAD : Left anterior descending artery

LBBB : Left bundle branch block

LCX : Left circumflex artery.

LIMA : Left internal mammary artery

LV : Left ventricle.

LVEF : Left ventricular ejection fraction

MI : Myocardial infarction

MIBI : Methoxyisobutyl isonitrile

M-Mode : Motion mode

MRI : Magnetic resonance imaging.

MSCT : Multislice computed tomography

No : Nitric oxide

No. : Number

PCI : Percutaneous coronary intervention

PDA : Posterior descending artery

PET : Pitrson emission tomography.

PT : Patient

RCA : Right coronary artery

RSTD : Remote ST segment depression.

RV : Right ventricle

SD : Standard deviation

SPECT : Single- photon emission computed tomography

TBI : Technetium Butly isonitrile

Tc-99m : Technetium 99m

TL-201 : Thallium-201

VEGF : Vascular endothelial growth factor

Dedication

To The Soul of My Grand Father
To The Soul of My Mother
To the Soul of My Father
To My Sister & Brother

INTRODUCTION

Coronary heart disease is a leading cause of death in adults, accounting for more than one fourth of all deaths in individuals over the age of 35 years. (Montbly ., 1989).

Patients with chronic coronary artery disease and chronic total occlusion are defined as TIMI 0 are TIMI 1 type flow in the artery for more than three months. They have a more severe course of coronary artery disease. Thus, they more often suffer myocardial infarction and high grades of angina. Myocardial function is much more affected if there is occlusion of the left anterior descending artery or there are no signs of callaterals. (Savchento et al., 2000).

Stress myocardial perfusion study is an important component of clinical evaluation, stratification and management of these patients. Tc-99m sestamibi and thallium imaging have similar accuracy when used for assessing myocardial viability. (Maddahi et al., 1990).

Because of long half life of TI-201 which limits the injected dose of 3 to 4 Mci resulting in relatively low count density of images. This has encouraged the development and clinical testing of several Tc-99 m labeled myocardial perfusion tracers. (**Sinusas et al., 1990**).

Tc-99m sestamibi, like TI- 201 is positively charged particle, but its transport across the cell membrane is not dependent on ATP due to its high lipophilicity. Once inside cells, it is predominantly (84%) bound to the mitachondria and is directly related to myocardial blood flow over a wide range of flow rates with a "roll- off" in uptake occuring at high flow rates similar to that observed with TI- 201. (**Jones et al., 1990**).

1

At low flow rates Tc-99m sestamibi overestimates myocardial blood flow. This effect is most pronounced in myocardium with significant collateral flow and preserved viability, consistent with overextraction or redistribution of the tracer. This is markedly decreased in non viable myocardium regardless of blood flow. (Chareonthaitawee et al., 2000).

By convention when interperting myocardial perfusion SPECT study, reversible perfusion defects are considered to be ischemic areas. Irreversible perfusion defects (Sinusas et al., 1989) are described as representing scars of previous infarction. Moreover, partially reversible perfusion defects are usually considered as representing scars of infarction with surrounding ischemia (peri- infarct ischemia).

However, during our work at nuclear cardiology laboratory in Ain Shams University Hospital, we have noticed that some patients with no evidence of any previous myocardial infarction showed partially reversible perfusion defects in their Tc-99m sestamibi scans. When these patients were referred for coronary angiography, it was found that these patients had chronic total occulsion of vessels supplying the region which showed partially reversible perfusion defects. Moreover, some of these patients underwent revascularization wetheter interventinally or surgically and were referred once more for myocardial perfusion imaging as follow up for their condition-post-revascularization. Strongely enough, these patiens with no evidence of restenosis showed normal myocardial perfusion denoting that these partially reversible perfusion defects which were present in their first scans did not represent infarction but instead a condition of severely reduced regional myocardial perfusion.