Original Article

Diagnostic Accuracy of Stress Myocardial Perfusion Imaging in Indian Diabetic Patients: A Single Centre Experience

Deepa Kumar, Ravinder Singh Sethi, Sandeep Bansal[1], Padma A Namgyal, Aditi Khurana Sehgal, Tajamul Syed Malik

Departments of Nuclear Medicine and [1]Cardiology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Abstract

Diabetics have around 2-4 times increased risk of coronary artery disease(CAD) and it is the most important cause of mortality in these patients. This study was carried out to compare the sensitivity, specificity and accuracy of MPI-SPECT among diabetics and non-diabetics in the Indian population. **Material and Methods:** This retrospective study included 261 patients; 213 males and 48 females, with 75 diabetic and 186 non-diabetic patients. Only type II diabetics and non-diabetic patients were included in the study. Only patients who had coronary angiography (CAG) done within 6 months of the stress ^{99m}Tc-sestamibi MPI-SPECT study were included in the study. Two arbitrary cut off points on CAG ≥ 50% and ≥ 70% were used for determination of extent of CAD. **Results:** Considering coronary angiography as gold standard with ≥ 50% coronary stenosis as a cut off criteria for significant stenosis the sensitivity and specificity respectively, of myocardial perfusion SPECT was 83% and 72% in diabetics and 81% and 69% in non-diabetic pateints (*p* value not significant). For ≥ 70% coronary stenosis as a cut off criteria for significant stenosis the sensitivity and specificity respectively, of myocardial perfusion SPECT was 87% and 61% in diabetics and 88% and 58%in non-diabetics (*p* value not significant). No significant difference was found in the sensitivity, specificity and accuracy of LAD, LCx and RCA coronary vessels among diabetics and non-diabetics for both ≥ 50% and ≥ 70% coronary stenosis as cut off criteria. Diabetic patients had a lower incidence of SVD compared to the non-diabetic patients. They also had a higher incidence of TVD and MVD compared to the non-diabetic patients with both ≥ 50% and ≥ 70% diameter stenosis criteria (*p* value significant). **Conclusion:** Sensitivity and specificity of ^{99m}Tc-sestamibi myocardial perfusion imaging is similar in diabetic and non-diabetic patients in Indian population.

Keywords: *Coronary angiography, coronary artery disease, diabetic, myocardial perfusion SPECT*

Introduction

The prevalence of type II diabetes is significantly increasing[1] and is on the verge of becoming a pandemic in India.[2,3] In a study conducted in 2007, around 135 million people had diabetes worldwide and of these, India had a total of 40.9 million diabetics.[4] Type II diabetes has several risk factors in common with coronary artery disease (CAD), such as age, hypertension, hyperlipidemia, obesity, physical inactivity and stress, hence an increase in the prevalence of diabetes is indirectly related with increased risk of CAD.[2,5] Diabetics have around 2-4 times increased risk of CAD and CAD results in more than 80% of all deaths and 75% of all hospitalizations in diabetic subjects.[2,5-7] Myocardial ischemia in diabetics may occur due to microvascular disease, rather than epicardial coronary stenosis that is characteristic of atherosclerotic CAD.[8] Diabetics have altered coronary vasoreactivity and non-atherosclerotic microvascular abnormalities.[9]

Myocardial perfusion imaging (MPI) single photon emission computed tomography (SPECT) being a non invasive test plays an important role in the detection of coronary artery disease.[10] Study has been done to compare the diagnostic accuracy of SPECT MPI in diabetic and non diabetic patients by Kang etal.[10] But as the demographic profile of the Indian population differs from the Caucasian population and there is scarcity of similar studies performed in Indian population, hence, this study was designed to evaluate the sensitivity and specificity of stress ^{99m}Tc-sestamibi MPI-SPECT in diabetic

Address for correspondence:
Dr. Ravinder Singh Sethi, Senior Specialist and Head, Department of Nuclear Medicine, Safdarjung Hospital and Vardhman Mahavir Medical College, New Delhi - 110 029, India.
E-mail: rssethi@yahoo.com

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patients and compare it with the non-diabetics patients in Indian population, with coronary angiographic data used as gold standard for detection and quantification of coronary artery disease.

Material And Methods

This was a retrospective study. The patients referred to department of Nuclear Medicine for stress MPI-SPECT between January 2010 and August 2016 were included in this study. Only type II diabetics and non diabetic patients were included in the study. Type I diabetics were not included in the study. The population for the study included 261 patients; 213 males and 48 females. Out of the 261 patients included in the study, 75 were diabetic and 186 were non-diabetic. The forms of stress performed were exercise or pharmacological (dobutamine or adenosine infusion). Out of the 75 diabetic patients included in the study, 24 patients underwent exercise, 16 adenosine and 35 dobutamine stress. Out of the 186 non-diabetic patients included in the study 73 underwent exercise, 43 adenosine and 70 dobutamine stress. The stress was given to the patient in the presence of a cardiologist and stress ECG was reported by the cardiologist only. The patients who had coronary angiography (CAG) done within 6 months of the stress ^{99m}Tc-sestamibi myocardial perfusion SPECT study were included in the study. The angiograms were interpreted by experienced cardiologists. Patients with documented history of infarction, coronary artery bypass grafting, pathologic Q waves on ECG, left bundle branch block or non-ischemic cardiomyopathy were not included. The patients who had any cardiac event between MPI-SPECT and CAG were excluded from the study. Beta blockers were stopped for 3 days prior to the test.

Imaging protocol for Stress myocardial perfusion

The study was conducted as a two day protocol stress followed by rest. Around 10mCi of ^{99m}Tc-sestamibi was administered intravenously at peak stress for the stress study and on day 2 for the rest study. The SPECT acquisition was done on Philips Precedence dual head SPECT gamma camera with parallel hole, low energy high resolution collimator with 64 projections at the rate of 30 seconds per projection using 64x64 matrix. A 20% window centred on 140keV photopeak was selected. Gated SPECT was acquired at 16 frames per cycle with 180degree arc with continuous step and shoot method from 45 degree right anterior oblique to 45 degree left anterior oblique. Processing was done using Autospect and Autoquant softwares, using butterworth filter order 5. Short axis, horizontal long axis and vertical long axis slices were obtained. Stress and rest images were compared.

Image analysis and diagnostic criteria

The interpretation of the MPI-SPECT was done by 2 experienced nuclear medicine physicians independently. Each vascular territory was either categorized as normal or abnormal having a perfusion abnormality. The perfusion defect which showed complete reversibility on rest image was considered to be ischemia. A perfusion defect on the stress image which did not show any change in the rest image was considered as a fixed defect. A perfusion defect on stress image which showed incomplete reversibility was considered as a mixed defect. Fixed defects with normal wall thickening and normal wall motion were considered to be due to soft tissue attenuation and labelled as normal Further categorization of perfusion defect was based on the size of the left ventricular myocardium involved. Small defects had < 5%, medium sized defects 5-10% and large sized defects had >10% of the left ventricular myocardium involved.[11] Each defect was assigned to one of the three major coronary artery territories.

CAG was performed with the Saldinger's approach. Two arbitrary cut off points ≥ 50% and ≥ 70% maximal lumen diameter narrowing, were used for determination of extent of coronary artery disease.[10,12,13]

The statistical tests used were the Student 't' test, or, the Chi square test. Continuous data was presented as mean ± S.D. and compared with the student 't' test. Categorical data was compared with Chi-square test. Sensitivity (%) was calculated as 100 x True positive/True positive + false negative, Specificity(%) as 100 x True negative/True negative + False positive and Accuracy(%) as 100 x True positive + True negative/total number of patients.

Patient characteristics

The patient characteristics and scan variables of diabetic and non-diabetic patients included in the study are shown in Table 1. Lipid profile was available in 41 diabetic and 124 non-diabetic patients. There was no significant difference in the age, sex distribution, hypertension, hyperlipidemia, obesity, sedentary life style, ischemic ECG changes between the diabetic and non-diabetic groups. The incidence of smoking was less in the diabetic group compared to the non diabetic group (*p* value 0.002). Duration of diabetes in the diabetic group ranged from 1-30 years (7.6 years ± 6.81). Out of the 75 diabetic patients, 65 were on oral hypoglycemic agents, 3 received combination of oral hypoglycemic agents and insulin and 7 were on dietary modification and physical activity. According to American Diabetes Association standards of medical care in diabetes 2016 guidelines, a reasonable HbA1c goal for non pregnant adults is below 7%.[14] HbA1c data of diabetic group in our study revealed that 54(72%) of the diabetic patients had well controlled diabetes (HbA1c < 7%), while 21 (28%) of the patients had poorly controlled diabetes (HbA1c ≥ 7%). So the present study was done on a majorly controlled diabetic group receiving treatment for diabetes.

Angiographic characteristics and MPI-SPECT findings

Angiographic characteristics of the diabetic and non-diabetic patients are shown in Table 2. A total of 225 coronary arteries were examined in 75 diabetic patients and 558 coronaries in 186 non-diabetic patients. Diabetic patients had a lower incidence of single vessel disease (SVD) compared to non-diabetics. For ≥ 50% diameter stenosis criteria, the incidence of SVD was 35% in diabetics and 45% in non diabetics but no significant difference was found statistically. For ≥ 70% diameter stenosis criteria, the incidence of SVD was 28% in diabetics and 46% in non-diabetics (*p* value 0.007) and the difference was statistically significant. Multivessel disease (MVD) includes both double vessel (DVD) and triple vessel diseases (TVD).[10] Diabetics had a higher incidence of TVD and MVD compared to the non diabetic patients with both ≥ 50% and ≥ 70% diameter stenosis criteria (*p* value significant).

Comparison of extent of coronary stenosis and size of perfusion defect in diabetic and non-diabetic patients is depicted in Table 3 and Table 4 respectively. In the diabetic group, 225 coronaries were examined out of which 72 coronaries were normal, 21 coronaries showed < 50% coronary artery stenosis (CAS), 27 coronaries 50-70% stenosis and 105 coronaries > 70% stenosis. In the non diabetic group, 558 coronaries were examined out of which 223 coronaries were normal, 53 coronaries showed < 50% CAS, 105 coronaries 50-70% stenosis and 177 coronaries > 70% stenosis.

In the diabetic group, with ≥ 50% stenosis, 22 coronaries had normal finding on MPI-SPECT, 13 showed small defects and 97 showed moderate to large perfusion defects. The proportion of moderate to large perfusion defects in coronaries with > 50% stenosis was 73.5% in this group. In the non-diabetic group, with ≥ 50% stenosis, 54 coronaries had normal finding on myocardial perfusion SPECT, 45 showed small defects and 183 showed moderate to large perfusion defects. The proportion of moderate to large

Table 1: Patient parameters, stress ECG and MPI data of diabetic and non-diabetic patients included in the study

Variable	Diabetics (*N*=75)	Non diabetics (*N*=186)	*P* value
Age (years)	57.81±10.3 (Range 30-78)	55.18±11.51 (Range 30-86)	0.08
Female	16 (21%)	32 (17%)	0.44
Male	59 (79%)	154 (83%)	0.44
Hypertension	49 (65%)	109 (59%)	0.37
Smoking	19 (25%)	84 (45%)	0.002
Hyperlipidemia	14/41 (34%)	38/124 (31%)	0.72
Sedentary lifestyle	49 (65%)	125 (67%)	0.75
Obesity	26 (35%)	62 (33%)	0.75
Ischemic changes on stress ECG	22 (29%)	38 (20%)	0.11
TID	10 (13%)	30 (9%)	0.33
Ischemia on MPI-SPECT	22(29%)	52 (30%)	0.87
Fixed defect on MPI-SPECT	20 (27%)	68 (37%)	0.12
Mixed lesion on MPI-SPECT	29 (39%)	53 (28%)	0.08
Normal study on MPI-SPECT	4 (5%)	13 (7%)	0.55

Table 2: Diabetic and non-diabetic patient's CAG findings

	≥50% coronary stenosis		≥70% coronary stenosis	
	D *N*=75	ND *N*=186	D *N*=75	ND *N*=186
Normal / minor CAS	3 (4%)	14 (7%)	13 (17%)	37 (20%)
SVD	26 (35%)	84 (45%)	21 (28%)	86 (46%)*
DVD	23 (30.5%)	54 (30%)	23 (31%)	43 (23%)
TVD	23 (30.5%)	34 (18%)*	18 (24%)	20 (11%) *
MVD	46 (61%)	88 (48%)*	41 (55%)	63 (34%)*

p not significant for all comparisons of diabetes to no diabetes except marked as*, **p* value <0.05, D=Diabetic, ND=non-diabetic, CAS=coronary artery stenosis, SVD=Single vessel disease, DVD=Double vessel disease, TVD=Triple vessel disease, MVD=Multivessel disease

Table 3: Diabetic patient's data of CAG vs MPI-SPECT findings in corresponding vascular territories

	Normal coronary	<50% CAS	50-70% CAS	>70% CAS
Normal	55	12	8	14
SD	11	3	5	8
MD	6	5	9	29
LD	0	1	5	54

CAS=coronary artery stenosis, SD=small defect, MD=moderate defect, LD=large defect perfusion defects in coronaries with > 50% stenosis was 65% in this group.

Though MPI-SPECT had shown fixed perfusion defects in 27% diabetic and 37% non-diabetic patients, yet no significant difference was found statistically [Table 1]. The incidence of mixed perfusion defects was more in the diabetic group (39%) as compared to the non-diabetic group(28%) with no significant difference statistically [Table 1]. The incidence of ischemia on MPI-SPECT has been found to be similar in diabetic and non-diabetic groups [Table 1].

MPI-SPECT in diabetic and non diabetic patients

Considering coronary angiography as gold standard and with ≥ 50% CAS as the cut off criteria for significant stenosis, the sensitivity of MPI-SPECT was 83% in diabetics vs. 81% in non-diabetics. The specificity was 72% in diabetics compared to 69% in the non-diabetic group [Table 5].

For ≥70% CAS as cut off criteria for significant stenosis, the sensitivity of MPI-SPECT was 87% in diabetics vs. 88% in non-diabetics. The specificity was 61% in diabetics compared to 58% in the non diabetic group [Table 5].

No significant difference was found in the sensitivity and specificity of MPI-SPECT among diabetic and non diabetic patients for both ≥ 50% and ≥ 70% stenosis as cut off criteria.

Sensitivity and specificity among male, female patients in the diabetic and non-diabetic patients

No significant difference was found in the sensitivity and specificity of MPI-SPECT among diabetic and non-diabetic male as well as diabetic and non-diabetic female patients for both ≥ 50% and ≥ 70% stenosis as cut off criteria [Table 6]. The sensitivity of MPI-SPECT in the diabetic and non-diabetic males for 50% stenosis as cutoff criteria was 86% and 80% respectively and specificity 74% and 70% respectively. No significant difference was found in the sensitivity and specificity of MPI-SPECT in detecting coronary artery disease in diabetic and non-diabetic males. The sensitivity of MPI-SPECT in the diabetic and non-diabetic females for 50% stenosis as cutoff criteria was 74% and 83% respectively and specificity 67% and 63% respectively. No significant difference was found in the sensitivity and specificity of myocardial perfusion SPECT in detecting coronary artery disease in diabetic and non-diabetic

Table 4: Non-diabetic patient's data of CAG vs MPI-SPECT findings in corresponding vascular territories

	Normal Coronary	<50% CAS	50-70% CAS	>70% CAS
Normal	169	20	32	22
SD	36	20	23	22
MD	18	13	28	39
LD	0	0	22	94

CAS=coronary artery stenosis, SD=small defect, MD=moderate defect, LD=large defect

Table 5: MPI-SPECT sensitivity (%) and specificity (%) comparison among diabetic and non-diabetic patients

	D	ND	*p* value
≥50% CAS			
Sensitivity	83	81	0.51
Specificity	72	69	0.4
≥70% CAS			
Sensitivity	87	88	0.69
Specificity	61	58	0.6

CAS=cornary artery stenosis

Table 6: MPI-SPECT sensitivity (%) and specificity (%) comparison in male and female population among diabetic and non-diabetic patients

	Males		Females	
	D	ND	D	ND
≥50% CAS				
Sensitivity	86	80	74	83
Specificity	74	70	67	63
≥70% CAS				
Sensitivity	86	88	93	86
Specificity	64	55	59	55

p value not significant for all comparisons of diabetes to no diabetes, D=Diabetic, ND=non-diabetic, CAS=coronary artery stenosis

Table 7: MPI-SPECT sensitivity(%), specificity%) and accuracy (%) for 3 major coronary vessels among Diabetic and Non diabetic patients for ≥ 50% coronary artery stenosis

	Sensitivity		Specificity		Accuracy	
	D	**ND**	**D**	**ND**	**D**	**ND**
LAD territory	90	80	65	64	83	74
LCx territory	76	77	76	74	76	75
RCA territory	82	85	73	66	77	75

p value not significant for all comparisons of diabetes to no diabetes, D = Diabetic, ND = non-diabetic

Table 8: MPI-SPECT sensitivity(%), specificity%), accuracy (%) for 3 major coronary vessels among Diabetic and Non diabetic patients for ≥ 70% coronary artery stenosis

	Sensitivity		Specificity		Accuracy	
	D	**ND**	**D**	**ND**	**D**	**ND**
LAD territory	95	91	51	53	75	68
LCx territory	79	81	69	67	75	71
RCA territory	85	90	67	55	73	65

p value not significant for all comparisons of diabetes to no diabetes, D=Diabetic, ND=non-diabetic

females. The specificity of MPI-SPECT was little higher in the diabetic females, but *p* value was non-significant.

Sensitivity, specificity and accuracy of 3 major coronary vessels

For ≥ 50% and ≥ 70% coronary stenosis as cut off criteria the sensitivity, specificity and accuracy of 3 major coronary vessels among diabetic and non-diabetic patients is illustrated in Table 7 and Table 8 respectively.

No significant difference was found in the sensitivity, specificity and accuracy of LAD, LCx and RCA coronary vessels among diabetics and non-diabetics for both ≥ 50% and ≥ 70% coronary stenosis as cut off criteria.

Discussion

Diabetic patients have increased risk of CAD[4-6] and ^{99m}Tc-Sestamibi MPI-SPECT is a well documented imaging modality for the detection and prognostication of CAD. [10] This study showed that MPI-SPECT has similar sensitivity and specificity in both diabetic and non-diabetic group. In the diabetic group, the sensitivity for detection of CAD (83% for 50% CAS and 87% for 70% CAS) was similar to the non-diabetic group (81% for 50% CAS and 88% for 70% CAS) (*p* value non-significant). The specificity was also similar in the diabetic and non-diabetic group. No significant difference was found in the sensitivity, specificity and accuracy for detection of individual diseased coronary vessel between the diabetic and non-diabetic groups for both 50% and 70% coronary stenosis as cut off criteria for significant CAD.

This is one among the very few studies done to compare the sensitivity and specificity of MPI-SPECT between the diabetic and non-diabetic group in the Indian population.

Kang *et al.*[10] compared sensitivity, specificity and accuracy of MPI-SPECT in patients with and without diabetes mellitus and found no significant difference in the sensitivity, specificity of MPI-SPECT in the two groups. The sensitivity and specificity of MPI-SPECT for detecting CAD, with the criteria of 50% as significant stenosis were 86% and 56% in diabetics and 86% and 46% in non-diabetics in their study, with no significant difference noted statistically. The sensitivity, specificity and accuracy for individual vessel detection was also similar in the two groups, except for lower sensitivity and higher specificity for detecting left anterior descending coronary artery disease in the diabetic group. We found similar sensitivity in the diabetic and non-diabetic group and little higher specificity in both the diabetic and non-diabetic group. We found no significant difference in the sensitivity and specificity of MPI among the diabetic and non-diabetic group. But the *p* value was not significant. The sensitivity of stress MPI-SPECT for detecting LCx coronary artery disease was found to be low compared to the LAD and RCA coronary artery disease in both the diabetic and non-diabetic group in our study. The accuracy was also similar for detection of CAD in individual vessels in the diabetic and non-diabetic group with no significant difference noted statistically in our study. The possible reason for this finding could be due to the fact that assigning a perfusion defect to a specific territory is arbitrary and there may be overlap in the distribution of blood supply. Some defects of the LCx territory may have been misclassified as the defects of the LAD or the RCA territory.[10]

In this study diabetics had a higher incidence of TVD and multi-vessel disease compared to the non-diabetics for both the 50% and 70% stenosis as cut off criteria. The incidence of moderate to large perfusion defects with ≥ 50% stenosis in diabetics was found to be higher (73.5%) than the non-diabetics (65%), so the severity of the disease was more in the diabetic group compared to the non-diabetic group, consistent with a higher incidence of triple vessel and multi-vessel disease in the diabetic group in our study.

Harshad K *et al.*[11] evaluated the prevalence of asymptomatic CAD in asymptomatic diabetics by MPI-SPECT. In comparison to CAG, the sensitivity of MPI-SPECT was 86.6% and specificity 52%. Our study has been done in symptomatic diabetics. The sensitivity of MPI-SPECT for detecting CAD in symptomatic diabetics in our study was similar to this study, however specificity of MPI-SPECT in diabetics was a little high (72% specificity for ≥ 50% coronary stenosis used as the cut off criteria) in our study.

Loong *et al.*[15] found a sensitivity of 86% and specificity of 74% of myocardial perfusion SPECT in diagnosis of CAD. The results of our study in both the diabetic and non-diabetic group are consistent with this study.

Very few studies have been done to compare the sensitivity and specificity of MPI-SPECT in diabetic and non-diabetic patients using coronary angiography data as gold standard. Nesto *et al.*[16] did a study to compare angina and myocardial ischemia among diabetic and non-diabetic patients using exercise thallium scintigraphy with no coronary angiography data available. They compared 50 diabetic and 50 non-diabetic patients, all with ischemia on exercise thallium scintigraphy. The two groups had similar clinical characteristics, treadmill test results and extent of ischemia, but only 14 patients with diabetes had angina during exertional ischemia compared to 34 non diabetic patients. So, they stated that thallium scintigraphy is a better tool to assess the extent of ischemia in patients with diabetes as compared to clinical evidence of angina.

According to Shawgi M *et al.*[17], the combined use of attenuation correction with gated SPECT study would be most useful in ruling out attenuation artifacts. The authors found that there is an increase in the 'normal' interpretation category when attenuation correction is used with ECG gating compared to gated MPI or MPI alone.

Attenuation correction was not done in this study, but for fixed perfusion defects appearing as soft tissue attenuation artifacts, gated SPECT was analyzed to look for wall thickening and wall motion abnormality. Such fixed defects with normal wall thickening and normal wall motion were considered to be due to soft tissue attenuation and labelled as normal. Still some error in the specificity and accuracy is expected in this study.

According to Iskandar A *et al.*[18], attenuation correction, gated SPECT, prone imaging all can improve the specificity of SPECT. Attenuation correction was not done in any of the studies included in their analysis and gated SPECT was done only in four studies. They suggested that with the application of these techniques the diagnostic accuracy of SPECT MPI may be better in both genders than reported in their analysis based on available literature.

Felsher *et.al.*[19] evaluated the prognostic value of thallium MPI in patients with diabetes mellitus. They included 123 patients with DM. 56% of the patients had abnormal thallium images. During follow up (lasting upto 36 months), there were 12 cardiac events, four patients died of cardiac events and 8 had non-fatal acute myocardial infarction. They concluded that exercise thallium imaging is useful in risk stratification of patients with diabetes mellitus.

The incidence of smoking in the diabetic group was low (25%) compared to the non-diabetic group (46%) (*p* value significant). The possible reason for this could be that diabetic patients were advised to quit smoking at the time of detection of diabetes and since they might have left smoking few years back, hence, negative history of smoking.

The incidence of Transient Ischemic Dilation of left ventricular cavity and ischemia was comparable in the diabetic and non-diabetic group (*p* value non-significant) in our study.

The incidence of ischemia on MPI-SPECT has been found to be similar in diabetic and non-diabetic groups. The incidence of fixed perfusion defects in diabetic patients was less compared to the non-diabetic patients. This high incidence of fixed defects and ischemic lesions in non-diabetic patients could be due to referral bias as non-diabetic patients with suspected or known CAD were sent to our department.

Limitations:

As only patients with no previous history of myocardial infarction and revascularization were included in the study, so the patients in this study represent a true diagnostic population. Hence, the findings of the study may not be applicable to a broader population presenting with infarction or those who have undergone intervention.

Type I diabetics were not included in this study. Type I diabetics are usually young, non obese and have normal lipid values. Whether myocardial perfusion SPECT study performs equally well in Type I and Type II diabetics would need a further study.

Conclusion

The results of this study show that myocardial perfusion SPECT has similar sensitivity and specificity for detection of CAD in the diabetic and non-diabetic patients. This non- invasive diagnostic test appears to be as valuable for detection of CAD in diabetes, as in the non-diabetics.

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Conflicts of interest

There are no conflicts of interest

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