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Persantin Myocardial Perfusion Imaging for The Detection of Ischemia in Asymptomatic Diabetic Saudi Patients (DIADS)

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Abstract

Background: Vascular complications occur in diabetic patients and more frequent when diabetes mellitus (DM) is uncontrolled. Among these complications are coronary artery diseases, which may lead to asymptomatic ischemic heart disease (IHD). The aim of this pilot study is to determine the prevalence of silent ischemia among Saudi patients with type 2 DM.

Results: A retrospective cohort study analyzing myocardial perfusion imaging (MPI) in Saudi patients with type 2 DM investigated for the presence of silent IHD. They had DM at least for 5 years duration and not less than 2 cardiovascular risk factors with no signs, symptoms or history of IHD. The mean age of the total cohort (n=490) was 62.2±11 years, 299 females (61%) and 191 males (39. Persantin MPI was positive in 237 patients (48.4%) and only 158 of them had coronary angiography of whom 33 (21%) had significant coronary anatomic lesions.

Conclusion: The prevalence of silent ischemia among asymptomatic Saudi patients with type 2 DM was 21%, which means that more than 2 out of 10 patients had silent myocardial ischemia. However and in order to justify the use of stress MPI as a screening test in this group of patients, a prospective large national study including both controlled and non-controlled type 2 DM is required.

Keywords: Saudi; Diabetics; Asymptomatic; Silent Ischemia; DIADS

List of Abbreviations: MIBI: technetium (99mTc) sestamibi; SSS: summed stress score; SRS: summed rest score; SDS: summed difference score; TID: transient ischemic dilation; LVEF: left ventricular ejection fraction

Introduction

Diabetes mellitus (DM) is a major cause of cardiovascular morbidity and mortality worldwide [1]. The prevalence of DM worldwide has been estimated to be 200 million as of 2007 and to 300 million in 2025 [2] In a national epidemiological survey conducted in Saudi Arabia between 1995 and 2000, the prevalence of DM was 23.7%, one of the highest in the world [3]. Diabetic patients have more extensive atherosclerosis and a higher prevalence of multi-vessel coronary artery disease (CAD), as well as higher silent myocardial ischemia and infarction rates, than non-diabetics [4]. CAD is the leading cause of death among type 2 DM patients [1,5-8]. More than 50% of diabetics die of coronary artery disease [9]. The risk of cardiac death in patients with type 2 DM reported to be 2-4 times than non-diabetic patients [10-12]. Silent ischemia in these patient is of asymptomatic nature and clinical manifestation only discovered in advanced stage [10-13]. Silent ischemia reported to be as high as 22% in diabetics, with marked perfusion abnormalities in 6% of patients [14,15].

Myocardial perfusion imaging (MPI) is an accurate diagnostic tool for detecting the functional significance of obstructive CAD and estimating the burden of myocardial ischemia (16). The sensitivity and specificity of MPI in detecting CAD reported to be 86% and 74% respectively [11,15,16].

The present study aimed to determine the prevalence of silent ischemia in asymptomatic Saudi patients with type 2 DM using pharmacologic stress MPI.

Methods

Study population

This retrospective study included consecutive patients previously diagnosed with type 2 DM referred to King Khalid University Hospital (Riyadh –Saudi Arabia) from the diabetic center at King Abdel Aziz University Hospital (Riyadh –Saudi Arabia) for stress MPI to investigate a suspicion of silent myocardial ischemia. We reviewed studies of all patients performed between July 2010 and October 2015. In addition, each patient had completed the full pharmacologic stress protocol and had interpretable imaging data. We used the patients' medical records to obtain demographic data, medical history, medical therapies, and subsequent cardiac procedures.

The study population consisted of 490 patients; 299 females (61%) and 191 males (39%) asymptomatic Saudi patients with type 2 DM who had controlled DM for more than 5 years and at least two other risk factors such as hypertension and dyslipidemia. All patients had no symptoms or signs of ischemic heart disease. Patient age ranged from 40 to 70 years, 70 patients were less than 50 years old (14.3%) and 420 patients were more than 50 years old (85.7%).

Myocardial perfusion imaging protocol

All patients were instructed to stop their anti-angina medications, including β-blockers, calcium channel blockers, and long-acting nitrates, 48 hours prior to the stress date. The patients also asked to abstain from caffeinated beverages for 24 hours and to fast 6 hours prior to the test.

All patients underwent a one-day imaging protocol. Single photon emission computed tomography (SPECT) scan acquired as per the guidelines of the American Society of Nuclear Cardiology [17-19]. Patients underwent an intravenous weight-based dipyridamole (Persantine) infusion administered over 4 minutes. Vital signs (Blood pressure, heart rate) and ECG monitoring supervised by cardiology fellow during stress part of the study. The radioactive isotope used was technetium 99m-sestamibi. The radioactive isotope was injected at minute 4 of Persantin infusion. Technetium 99m-sestamibi (10 mCi) administered at the stress part of the study (The dose increased in overweight patients) done first, followed by 30 mCi given at rest. SPECT imaging was performed using a dual head gamma camera (Cardio MD, Phillips) for slim patients with additional prone images when diaphragmatic or breast artifact was there and images analyzed with AutoSPECT professional software without motion correction or attenuation correction software and SPECT low dose CT (Philips' BrightView XCT) for obese patients with attenuation correction. Butterworth filter and reconstruction using the filtered back projection method in all studies. Astonish reconstruction was used when time of imaging planned to be reduced due to patient condition or technical issues. Gated acquisition performed on the stress images in all patients except those with significant arrhythmia and high rejection rate.

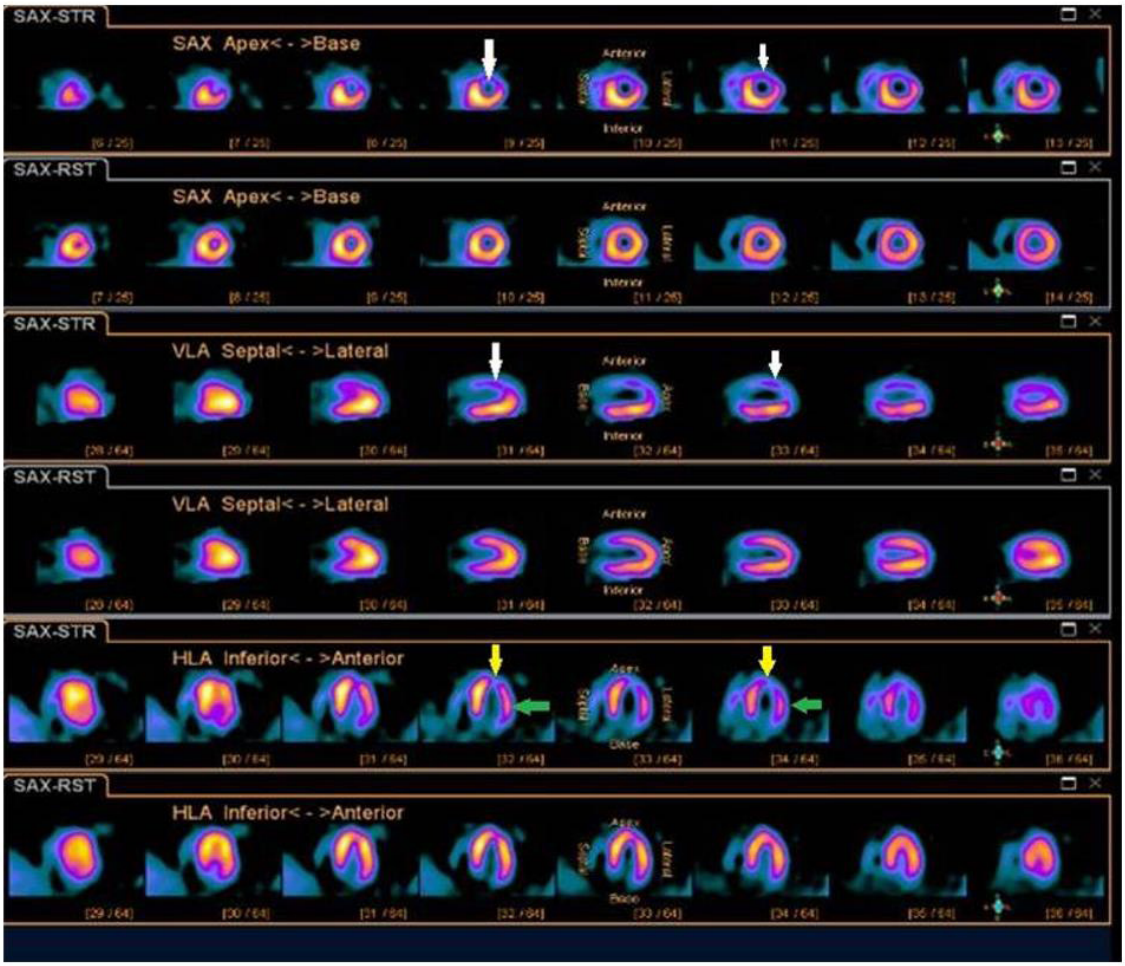
Statistical analysis: Categorical data summarized as absolute numbers and percentages ± standard deviation (SD).

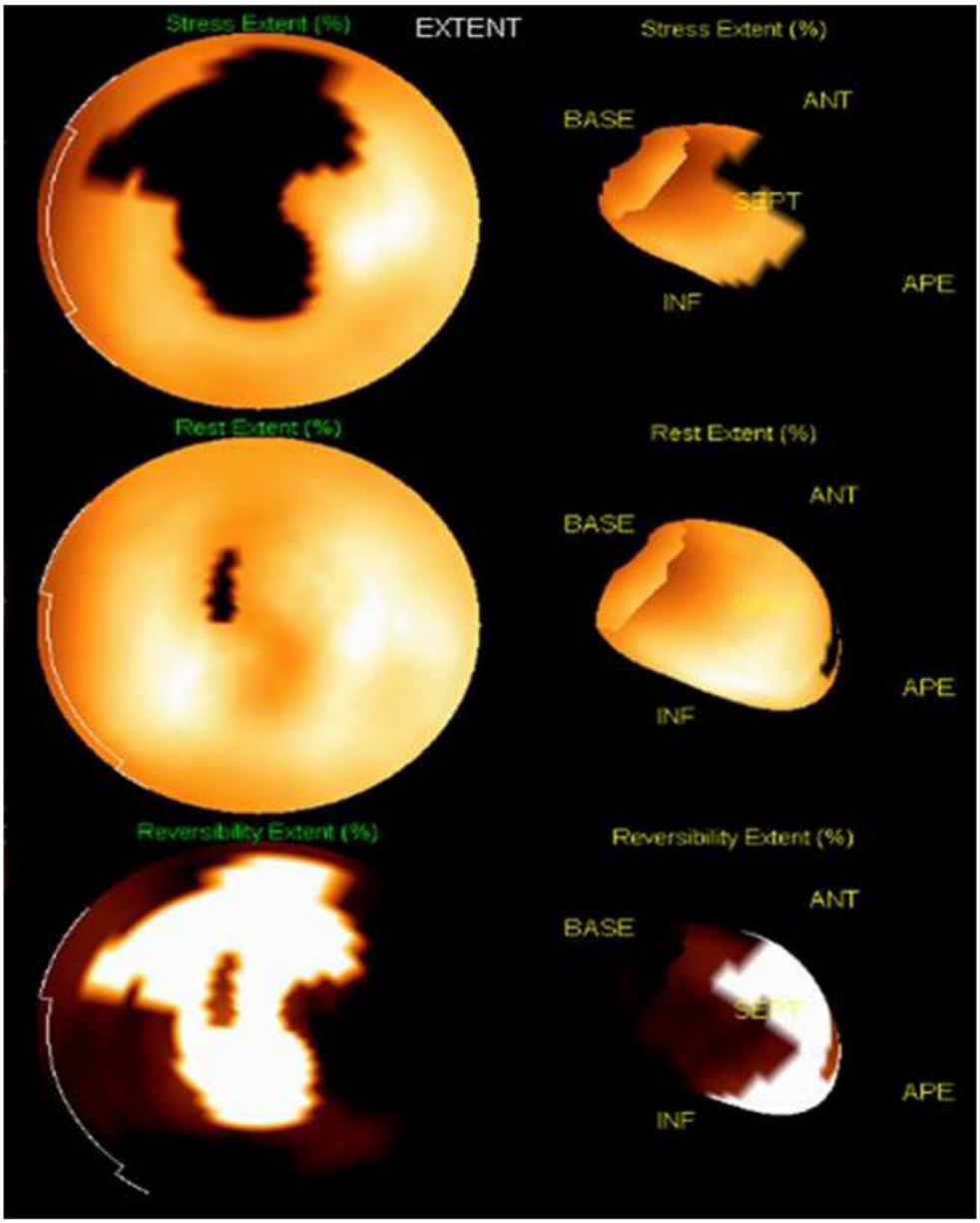
Results

Table 1 depicts the baseline characteristics of the study population.

Table 1: Patient characteristics of the study group

Clinical Characteristic	No.	%
Gender: Male	191	39%
Female	299	61%
Age: <50	70	14.3%
>50	420	85.7%
Weight: Normal (BMI <25.0)	38	7.8%
Overweight (BMI 25-30)	150	30.6%
Obese (BMI >30)	302	61.6%
B/P (Systolic) mmHg <130	64.0	13.1%
>130	426.0	86.9%
Total Cholesterol (mmol/L) <4.0	95	19.2%
>4.0	395	80.8%
Triglyceride (mmol/L) <1.7	234	48.5%
>1.7	256	51.5%
Fasting Blood Sugar (mmol/L) <10	67	10.6%
>10	423	89.4%




Stress Extent (%)
EXTENT
Stress Extent (%)
BASE
ANT
SEPT
APE
INF
Rest Extent (%)
Rest Extent (%)
BASE
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Reversibility Extent (%)
Reversibility Extent (%)
BASE
ANT
SEPT
APE
INF


TID 1.27
LHR 0.26
SSS 22 SRS 2 SDS 20
SS% 32 SR% 3 SD% 29
Proc ID Persantin Stress:MIBI
View ID SAX-STR
Date 2013-12-08 13:39:10
Database FemaleStressMB
Volume 85ml
Wall 152ml
Defect 57ml
Extent 38%
TPD 30%
Shape 0.61 [SI], 0.80 [Ecc]
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View ID SAX-RST
Date 2013-12-08 15:18:24
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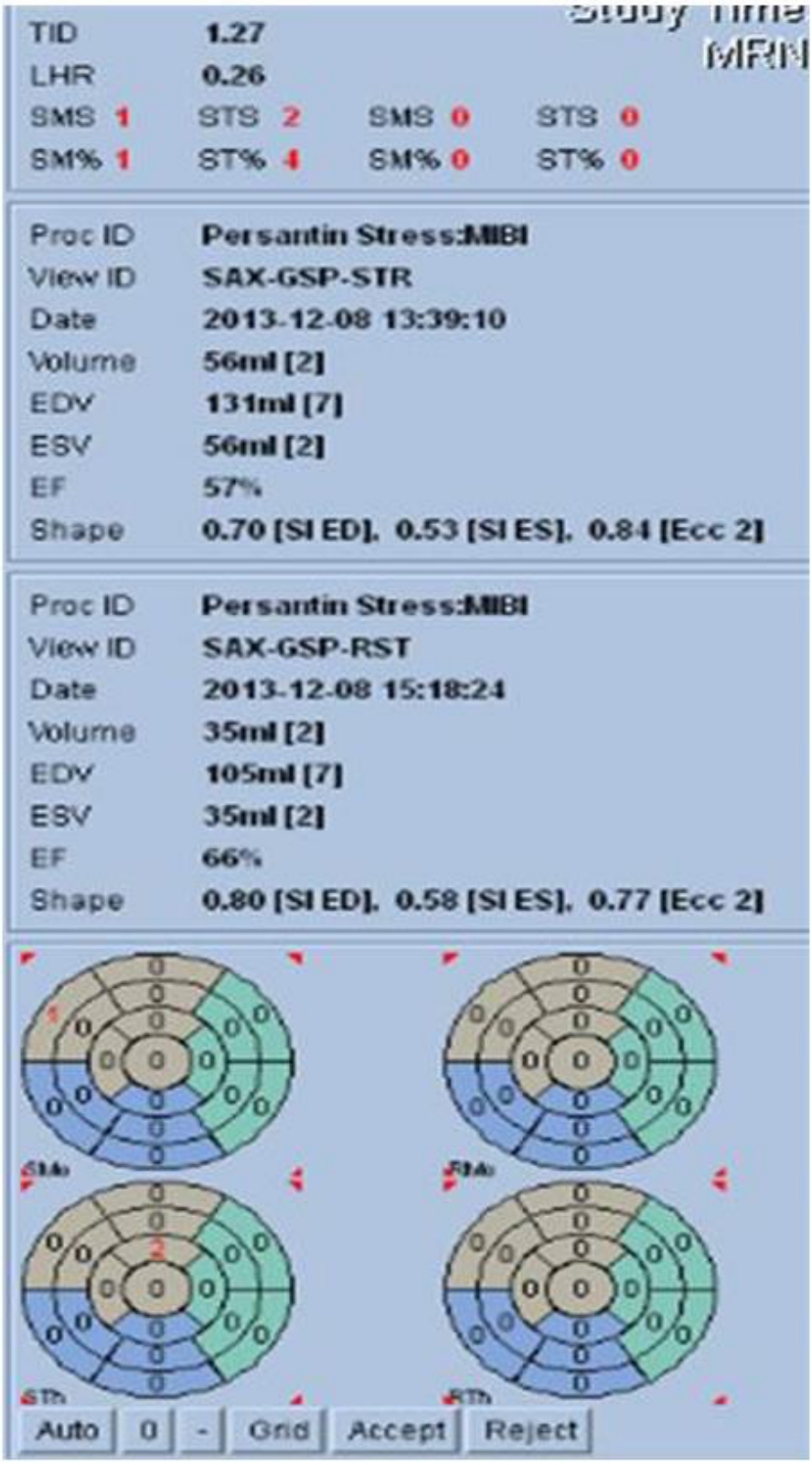

Figure 1: SPECT (Figure 1a): Stress induced ischemia (Arrows): anterior (white), apex (yellow) and antero-lateral wall (Green) shown on polar map (**Figure 1b).**

Semi quantitative data (Figure 1c): SSS = 22; SDS = 20 and Gated data (**Figure 1d)**: LVEF (66% at rest, 57% at stress).

Coronary angiography (not shown): 75% stenosis of left anterior descending coronary artery and 60% left circumflex

The presence or absence of ischemia reported, as well as its location in the left ventricular (LV) wall. To assess the severity of ischemia several parameters were derived from C-equal images in (Figure 1) of a 58-year-old male patient with DM, hypertension and dyslipidemia referred for persantin MPI to rule out stress induced ischemia): the summed difference score (SDS) was used. The SDS is the difference between two semi-quantitative scores for 20 LV wall segments: the summed stress score (SSS), which assesses the perfusion defect during stress with respect to severity and extent, and the summed rest score (SRS), which assesses the extent and severity of the perfusion defect during rest. This measure used to describe the degree to which the deficit/ischemia is reversible. Based on SSS the MPI was considered normal with value of (0-3), mild abnormal (4–8), moderate (9–13), and severe (>13). [Reversible perfusion defect is defined as SDS ≥2, mild stress induced ischemia (2–4), moderate (5–7), and severe (>7) [20].

In addition, the severity of ischemia assessed by the presence of transient ischemic dilatation (TID) with normal value of 1.22 and lung uptake expressed by lung to heart ratio (LHR) with normal value of 0.44. The left ventricular ejection fractions (LVEFs) at rest and stress also reported. All these parameters shown in Figure 1 as well.

Both qualitative and quantitative interpretation of imaging data carried by an expert in nuclear cardiology.

The final diagnosis of coronary artery disease based on coronary angiography according to a predefined protocol and interpreted by an experienced cardiologist.

The MPI findings shown in (Table 2). Our results showed the prevalence of silent myocardial ischemia in asymptomatic Saudi patients with type 2 diabetes mellitus was 21% and the positive predictive value of our MPI screening test 21%.

Table 2: Patient characteristics of the study group

Myocardial perfusion findings	**Total (n=490)**
Myocardial ischemia	237 (48.4%)
Coronary angiography	158 (66.7%)
Positive coronary angiography (coronary artery stenosis ≥50%)	33 (21%)
SSS	5.60 ± 10
SRS	4.1 ± 8.9
SDS	1.7 ± 2.9
TID	2 (1.0%)
LHR	0.3 ± 0.1
LVEF (rest), mean±SD	56.2 ±13.3
LVEF (stress), mean±SD	56.5± 14.1
LVEF difference, mean±SD	-0.4±15.9

Data are presented as n (%) and mean±SD

Abbreviations: SSS, summed stress score; SRS, summed rest score; SDS, summed difference score; TID, transient ischemic dilation; LHR; lung hear ratio, LVEF, left ventricular ejection fraction

Discussion

Patients with diabetes mellitus, in particular those with DM type 2 reported to be 2-4 times at higher risk of cardiovascular events when compared to non-diabetic partners [10,11, 21].

Stress radionuclide MPI used widely to evaluate patients with suspected or known ischemic heart disease. Several investigators have used MPI in the evaluation of patients with DM and reported high prognostic values [22-25]. Bax. J et al reported that MPI was valuable test for indentifying asymptomatic diabetic patient who might require early and aggressive intervention to manage their cardiovascular risk [21]. However, one important question needed to be answered and that which diabetic patients needed to be screened for coronary artery disease and which test to use? To answer that question Wackers et al from Yale University conducted a large multicenter study for the detection of ischemia in asymptomatic diabetics (DIAD) trial included 1123

participants with well-controlled type 2 DM and they had no symptoms suggestive of coronary artery disease. They found that the rate of silent ischemia on stress MPI was 22% [14].

Detection of ischemia in asymptomatic diabetic Saudi patients (DIADS) was the aim of this study conducted on patients attending a large diabetic center. None of them had symptoms of coronary artery disease and assumed a good sample of asymptomatic Saudi patients with DM type 2. Our results showed that more than 20% of those older than 50 years have silent ischemia correlates very well with the original DIAD study by Wackers, *et al.* [14]. However, that was unpredictable considering the high prevalence of type 2 DM among Saudi population. The optimal medical therapy in the intervening period between the decision to refer to MPI and the test date could be the cause of low prevalence of abnormal MPI in our cohort study. If that assumption is accepted then a higher prevalence rate of silent ischemia in both controlled and non-controlled type 2 DM expected in a future large national study.

Conclusion

The prevalence of silent ischemia among asymptomatic Saudi patients with type 2 DM found to be 21%, which means that more than 2 out of 10 patients had silent myocardial ischemia. However and in order to justify the use of stress MPI as a screening test in this group of patients, a prospective large national study including both controlled and non-controlled type 2 DM is required.

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