Correlation between transient ischemic dilatation (TID) and coronary artery disease in Saudi male patients

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Objective: **A high transient ischemic dilatation ratio (TID) for the left ventricle (LV) from a gated myocardial perfusion imaging (G-MPI) study is widely believed to be associated with significant coronary artery disease (CAD). We have investigated the relationship between TID and CAD for our male Saudi Arabian patient population.**

Methods: **In this retrospective study, all male Saudi Arabian patients who underwent a two-day G-MPI study using Tc99m MIBI during the year 2011 having a TID $\geqslant$ 1.20 were included. Quantitative perfusion and gated parameters were obtained using Cedar Sinai's AutoQuant software version 3.0, 2003, Means of summed stress scores, summed rest scores and summed difference scores (SSS, SRS, SDS, respectively), stress and rest ejection fraction (EF) were calculated. Visual interpretation was performed to classify the perfusion as normal, fixed, mixed (fixed and reversible defects), single reversible or multiple reversible defects. Coronary angiograms were assessed as normal with no CAD, single vessel, two-vessel or three-vessel disease. Correlations between the TID and other parameters were studied using analysis of variance (ANOVA) with IBM-SPSS version 20.**

Results: **A total of 52 male patients had a high TID of $\geqslant$1.20 (mean 1.30 ± 0.13). Ten patients had a SSS of 0–3 and 16 were classified as normal by visual assessment. Stress EF (mean 50.4 ± 12%) was lower than the rest EF (mean 56.6 ± 12.8%) with the difference being statistically significant (Students paired *t*-test, $p = 0.001$).**

Angiography results were available in 44 patients, 3 having a normal angiogram, 24 having three vessel disease, 7 having two vessel disease and 10 having one vessel disease. Five patients with normal perfusion and SSS = 0–3 had CAD as seen on a coronary angiography. CAD on coronary angiography showed a significant correlation with perfusion abnormalities as assessed by visual interpretation ($p = 0.002$). TID showed a significantly correlation with both perfusion abnormalities ($p = 0.009$), as assessed by visual interpretation, and with Summed difference scores, SDS ($p = 0.000$).

Conclusion: **A high TID on G-MPI was a very sensitive indicator of significant CAD. In patients with normal perfusion and high TID further workup is warranted.**

Keywords: Transient ischemic dilatation (TID), Gated myocardial perfusion imaging (G-MPI), Coronary artery disease (CAD), Ejection fraction (EF)

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Introduction

Gated myocardial perfusion imaging SPECT (G-MPI) after administration of Tc99m radiopharmaceuticals is an established procedure to diagnose CAD, assess the ischemia burden, stratify risk and evaluate response to treatment [1,2]. The SPECT projection data is gated by a trigger on the R wave of an ECG and each R–R interval is binned into time intervals. Gated MPI-SPECT enables assessment of functional parameters such as ejection fraction, wall motion and thickening as well as left ventricle volumes [3].

Several other parameters may also be derived from Gated MPI studies which have both diagnostic and prognostic significance. One of these is transient ischemic dilatation or TID. This is a comparison of the non gated LV cavity size on stress to rest. The usefulness of TID as a clinical tool for diagnosis and prognosis of CAD has been the subject of many studies [4–6]. It was found to be associated with the severity and extent of reversible or partially reversible perfusion defects [4]. The proposed underlying mechanisms of a high TID ratio include the presence of myocardial stunning as a possible cause of a true increase in LV size after exercise, pharmacologically-induced ischemia and a pseudo- dilation effect due to diffuse sub endocardial ischemia [4–8].

It is important to determine the cut-off value for an abnormal TID ratio. A literature review suggests that the cut-off value for an abnormal TID ratio will vary with patient population, gender, stressing modality, radiopharmaceutical, time from injection to imaging after stress, injected dose of the radiopharmaceutical on the rest and stress studies and the imaging protocol. Technical aspects of imaging such as the image matrix size, zoom and slice selection also may influence the calculation of TID [6]. The cut off value reported by various researcher range from 1.12 to 1.40 [4–9]. Most studies have reported that in male patients where normal LV EDV is >100 ml, when persantine pharmacologic stress is applied with a two day protocol and Tc99m tracers are used, a TID ratio of >1.19 is mostly abnormal [6–10].

Coronary artery disease is prevalent in Saudi Arabia [11]. While there have been several studies concerning TID ratio in different populations, to the best of our knowledge there has been no published study concerning a Saudi Arabian population. This study was designed to study the relationship between TID ratio as detected on G-MPI studies and severity of CAD as detected by G-MPI and angiography in a Saudi male patient population.

Abbreviations

TID	transient ischemic dilatation
CAD	coronary artery disease
SPECT	single photon emission computed tomography
G-MPI	gated myocardial perfusion imaging SPECT
SSS	summed stress scores
SRS	summed rest scores
SDS	summed difference scores
EF	ejection fraction
ANOVA	analysis of variance
SPSS	software package for statistical analysis
LV	left ventricle
EDV	end diastolic volume
ESV	end systolic volume
MBP	modified Bruce protocol
ECG	electrocardiogram
Tc99m MIBI	technetium 99m labeled sestamibi

Methods

Study design

This is a retrospective study. The nuclear medicine PACS records of Saudi male patients who underwent G-MPI from January 1, 2010 to December 31, 2011 were reviewed. Male patients who underwent both stress and rest G-MPI studies for known or suspected coronary artery disease and had transient ischemic ratio (TID) >1.19 were included in the study.

Demographic parameters (patient ID, age, reason for referral), stress testing parameters (type of stress, outcome of stress) and imaging parameters (pattern perfusion, perfusion abnormality and severity scoring, stress and rest left ventricle ejection fraction, transient ischemic dilatation ratio) were recorded on a data sheet. Angiography records were reviewed for angiography findings.

Exclusion criteria

Patients who had a non gated study due to atrial fibrillation, ventricular tachycardia or premature beats or an incomplete study due to technical reasons were excluded from the study.

Stress testing

Whenever possible, beta-blockers and calcium channel antagonists were terminated 48 h before testing and nitrates at least 6 h before testing. Patients were instructed not to consume coffee or other products containing caffeine for 24 h before the test. After 4–6 h of fasting the patient underwent either a physiological stress (modified Bruce protocol MBP) or a pharmacological stress (persantine or dobutamine). For dobutamine and

MBP the end points were either achieving at least 85% of the target heart rate (220-age in years) or ECG changes compatible with ischemia. For persantine stressing the end points were either completion of IV infusion over 4 min or ECG changes compatible with ischemia.

During both types of stress, the heart rate, blood pressure and a 12-lead electrocardiogram (ECG) were recorded at baseline and every minute thereafter. The ECG was monitored continuously (leads aVF, V1 and V5) for development of arrhythmia or ischemic ST-segment deviation. Blood pressure was measured and recorded at rest, at the end of each stress stage and at peak stress.

Image acquisition and processing

A stress MPI study was acquired first, where 25 mCi of Tc99m MIBI (Cardiolite TM) were injected IV at the stress end point. The patient was transferred to the nuclear medicine imaging room when their heart parameters had normalized.

For the rest study the patient underwent a second IV injection of 25 mCi of Tc99m MIBI under resting conditions.

A 180 degree of arc cardiac SPECT was acquired using ECG R–R gating on a dual head Philips ADAC Forte camera 2007 model. Each camera head acquired 32 frames with 8 bins per R–R interval. Projection data was displayed to checking for patient motion.

Reconstruction was carried out using filtered back projection (FBP) and then processed using Cedar Sinai's AutoQuant software version 3.0. Images were displayed, TID was derived as the ratio of the non gated LV cavity volume on stress to rest and a value >1.19 was considered abnormal.

Gated parameters (EF, EDV and ESV) were also derived. Briefly, this software provides quantitative scores defined from gender-specific normal limits by adding the scores from twenty left ventricular segments (0 = normal, 1 = mild, 2 = moderate and 3 = severe perfusion defect) on the stress and rest heart short axis images. The summed difference score (SDS) is the difference of SSS and SRS. The SSS is a quantitative measure of perfusion defect extent and severity. SRS is an index of the infarction and the SDS is a measure of the extent of ischemia. An automatic calculation of left ventricular endocardium volumes post-stress and at rest was obtained. The TID ratio is derived from the endocardial volumes as the ratio of the non gated left ventricular volume at stress divided by the non gated volume at rest. Left ventricular ejection fraction (LV-EF) was also derived.

Image interpretation

Interpretation of the images was performed by an experienced nuclear medicine physician. Images were categorized as normal, abnormal with fixed defect(s), abnormal with fixed and reversible defects, abnormal with reversible single or multiple defect(s).

Angiography results were interpreted by a cardiologist with extensive experience in coronary angiography. Patients were categorized according to severity of vessel involvement as normal, single vessel disease (SVD), two vessels disease (2VD) and three vessels disease (3VD).

Statistical Analysis

Statistical Analysis was carried out using SPSS software version 20. Means and SD of numerical parameter were calculated and testing for correlation between G-MPI and angiographic parameters was carried out using ANOVA. Statistical findings were considered significant if the p value was <0.05.

Results

The study consists of 52 patients of whom 44 underwent coronary angiography within 3 months of G-MPI. Means, ranges and SD of demographic features are summarized in Table 1.

Out of these 52 patients, the majority of the patients, 37, underwent persantine stress while 10 had dobutamine stress and 5 were stressed by exercise. The stress testing was positive in 8 patients only. This data is summarized in Table 2.

On visual interpretation 16 patients had normal perfusion, 10 patients showed predominately fixed defects representing infarction, 20 had single or multiple reversible defects and 6 showed a mix of fixed and reversible defects. These results are summarized in Table 3.

All patients had a TID of 1.20 or higher, range 1.20–1.86 with a mean of 1.30 ± 0.13. 25 of 52 pa-

Table 1. Demographic characteristics and G-SPECT parameters (total N = 52 male patients).

Parameter	Means	Standard deviation	Range
Age (years)	66.7	11.1	43–85
TID	1.30	0.13	1.20–1.86
Stress EF (%)	50.1	12	22–72
Rest EF (%)	56.4	12.8	22–83
EF differences (%)	−6	5	−18–2
SSS	9.3	8.6	0–35
SRS	3.6	5.5	0–21
SDS	5.7	5.4	0–23

Table 2. Type and results of stress test (total N = 52).

Stress type	Positive	Normal	Equivocal	Total
Persantine	6	24	7	37
Dobutamine	1	9	0	10
Exercise	1	3	1	5
Total	8	36	8	52

Table 3. Perfusion pattern (visual interpretation) (total N = 52).

Perfusion severity	Frequency
Normal	16
Infarction	10
Mixed	6
Single reversible defect	8
Multiple reversible defect	12
Total	52

Table 4. Coronary angiography findings; (total N = 44).

Findings	No of patients
Normal	3
One vessel disease	10
Two vessel disease	7
Three vessel disease	24

tients had stress EF <50%. 16 patients showed an improvement in EF of about 10% or more on the rest study. Angiography results were available in 44 patients and these are summarized in Table 4. Angiography results were normal in two patients and three vessel disease was reported in 24 of the 44 patients.

Discussion

Gated MPI-SPECT is widely used for detection of coronary artery disease and prognostic assessment of these patients. For prognostic assessment, perfusion scintigraphy has been used to assess disease extent and severity rather than the presence of disease itself [12–14]. A variety of indicators can be evaluated in this regard, including the extent and severity of perfusion defects, extent of reversible perfusion defects and transient ischemic dilation of the left ventricle [6,7,13–16].

Various studies have report the significance of a high TID. A high TID is purported to indicate severity of CAD and multi-vessel disease. Normal ranges of the TID varies among populations and depend upon the gender, type of stress, injection and imaging protocols, and radio pharmaceuticals employed [6–8].

In our study a total of 52 patients were included who had a high TID. The findings were correlated with angiographic results for 44 patients. Only three of these 44 patients had a normal angiogram while the majority (24/44) had 3 vessel disease. We used a TID ration of 1.19 as a cut off limit since our patient population comprised of males and a majority (37/52) were stressed according with persantine. Such a cut off has been reported by other investigators [4–6].

Stress ejection fraction was generally lower in this population and improved on the rest study. The TID ratio showed a strong correlation with severity of perfusion defects as detected by visual interpretation and with the summed difference scores ($p = 0.043$ and 0.009, respectively). These findings suggest that TID is related to the amount of inducible ischemia and this is in line with previously reported studies [5,6,16].

In this study there were three patients who had a high TID and normal angiograms. A high TID with no significant CAD on angiography has been reported in patients with left ventricular hypertrophy, hypertensive response during stress test and severe subendocardial ischemia [5,16–17]. In this study, one of the three patients with high TID and normal angiogram had left ventricular hypertrophy.

Sixteen of the 52 patients had a normal perfusion scan and high TID. Angiography was performed for only 9 of them. Two of these 9 patients had a normal angiography while the remainder had CAD. Five of these patients had a normal SSS score (0–3). There was only one patient with a high TID and perfusion abnormalities who had a normal angiogram.

The findings of this study re-emphasize the need of considering the significance of quantitative findings of TID and improvement in EF from stress to rest while reporting G-MPI. Abnormal TID even in presence of a normal perfusion carries a high likelihood of CAD. The most likely cause of the discrepancy between perfusion and quantitative TID ratio is balanced perfusion.

Limitations

This is the first attempt to study the relationship between TID and CAD in Saudi males. The number of patients included is modest. This study was conducted in male patients only. The number of female patients, during the study period, who had a high TID, was small (7 only). Of these seven patients none had undergone angiography. Hence this group was excluded from the study.

Recommendations

The study found that a high TID on Gated MPI-SPECT is a very sensitive indication of significant

CAD. In patients with normal perfusion and high TID further workup for CAD is warranted.

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