Angiographic results of the patients with positive transient ischemic dilatation on their gated myocardial perfusion imaging scans

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ABSTRACT

Objectives: Gated myocardial perfusion imaging (gMPI) is an established tool for the diagnosis and risk stratification of patients with coronary artery disease (CAD) providing a variety of parameters regarding to perfusion and function of left ventricle (LV). Transient ischemic dilation (TID) is one of them. The presence of TID has been shown as a marker of severe and extensive CAD. The aim of this study was to correlate scintigraphic and angiographic findings of patients with positive TID on their gMPI scans.

Methods: Stress-rest gMPI was performed for 27 patients with suspected CAD. TID was equal or higher than 1.03 (TID≥1.03) in all patients. All patients had invasive coronary angiography results during 3 months before or after their SPECT studies. Ejection fraction (EF), end-diastolic and end-systolic volumes (EDV, ESV), TID were calculated. We correlated angiographic results with scintigraphic findings of the patients with positive TID.

Results: We couldn't find statistical significant difference in functional parameters of the left ventricle between the groups of patients with normal or near normal coronary angiograms and with abnormal angiograms.

Conclusions: TID should be considered a high risk marker in clinical management of patients with suspected or known CAD. But it can also be positive in normal coronary angiograms of conditions such as hypertensive heart disease and hypertrophic cardiomyopathy. Therefore, TID should be correlated with other perfusion and functional parameters of LV to reach the final diagnosis. If it is the only finding, it is reasonable to be cautious while interpreting gMPI.

Introduction

Gated myocardial perfusion imaging (gMPI) is an established tool for the diagnosis and risk stratification of patients with coronary artery disease (CAD) and it's diagnostic and prognostic accuracy is excellent. gMPI provides a variety of parameters regarding to perfusion and function of the left ventricle (LV), and transient ischemic dilation (TID) is one of them. TID describes a phenomenon in which the size of the left ventricle is larger on the post-stress image than on the post-rest image and this has been reported for the first time on stress-redistribution thallium-201 scintigraphy (1). In true TID, the LV dilates during stress and remains dilated through the post-stress gMPI (2). The presence of TID of the LV on gMPI scan has been shown to be both a marker of severe and extensive coronary artery disease and a predictor of cardiac outcomes in independent studies (3, 4). It has been well documented that cutoff values for an abnormal TID vary widely throughout the literature, ranging from 1.012 to 1.36 (5). The stress induced dilatation of the LV was further supported by the findings in the preliminary report of the automatically measured SPECT TID ratio (6). When this ratio was derived from the epicardial edges of the LV, it was predictive of severe and extensive CAD, although less so than that derived from the endocardial edges (6).

The pathophysiology of ischemic LV dilatation is still unclear. Although, the theory of subendocardial ischemia gaining the widest acceptance (7), ischemia induced physical LV dilation post stress is another potential underlying mechanism (8). On the other hand, several studies have demonstrated that ischemic LV dilatation may be present in patients with normal perfusion and no significant epicardial coronary disease; for example in patients with hypertrophic cardiomyopathy, or in patients with hypertensive heart disease and left ventricular hypertrophy (9,10). Therefore the true diagnostic accuracy of TID on MPI is debated and the optimal threshold for its definition remains undefined. For this reason, the aim of study was to correlate the scintigraphic findings and angiographic findings of patients with TID on their gMPI scans.

Methods

Study Population

From January 2016 to September 2016, 27 patients (17 men,

70%, 10 women; age range: 44-78 years) who were referred to our department for stress-rest gMPI for suspected coronary artery disease were retrospectively enrolled to the study. The TID value of the LV on stress-rest-gMPI scans was equal or higher than 1.03 (TID≥1.03) in all patients of the study population and all patients had invasive coronary angiography results during 3 months before or after their SPECT studies. According to our acquisition protocols, a structured interview and clinical history were acquired, and cardiac risk factors were assessed before nuclear testing. All patients were instructed to discontinue beta-blockers, calcium antagonists, and nitrates at least 24 h before testing as a part of the routine nuclear cardiac testing. None of the patients have left bundle branch block, paced rhythm or fixed perfusion defects. Patients who have moved for any reason during the SPECT acquisition were also excluded from the study due to motion artefact. The hospital ethics committee approved the study protocol.

Stress Protocols

Of the 27 patients, 17 (70%) underwent exercise stress test and 10 (30%) adenosine (Apoteket Produktion&Laboratorier AB, Formvagen, Sweden) pharmacologic stress test. Symptom-limited treadmill exercise test according to the standard Bruce protocol (stepwise increments of velocity and slope every 3 min) with continuous 12-lead ECG assessment or adenosine (140 µgr/kg/min intravenously over 6 min) (11) were chosen on the basis of the patient's ability to exercise and to reach at least 85% of the maximal age-predicted heart rate. Of the 17 patients submitted to the exercise stress test, all of them reached at least 85% of the expected maximal heart rate.

Acquisition Protocol

All patients underwent two-day (stress-rest Tc-99m MIBI) protocol stress MPI. Following symptom-limited treadmill exercise using the standard Bruce Protocol, 259-74 MBq (7±2 mCi) of Tc-99m MIBI (Cardio-SPECT, Medi-Radiopharma, Budapest, Hungary) was injected intravenously at peak stress and on following day for rest SPECT imaging. The stress injection was performed when the patient reach the maximum exercise on treadmill or at 4 min after the onset of adenosine infusion. All acquisitions were initiated 30±15 min after the radiopharmaceutical injection while the patients were in supine position with arms placed over the head.

Daily quality control of the gamma camera was performed before starting the first study of the day in a routine fashion. The dedicated cardiac gamma camera (Discovery NM 530c, GE Healthcare, Haifa, Israel) was equipped with a multiple pinhole collimator and 19 stationary cadmium-zinc-telluride detectors. Each detector contained 32x32 pixelated 5-mm thick (2.46x2.46 mm) elements. A window of 15% was centered on the 140 keV gamma peak, and the gating was done with 16 frames per RR cycle. List mode files were acquired and stored. Images were reconstructed on the same workstation as for the standard SPECT acquisition (Xeleris II, GE Healthcare, Haifa, Israel) using a new dedicated iterative algorithm. A Butterworth postprocessing filter (frequency 0.37, order 7) was applied to the reconstructed slices. Images were reconstructed without scatter or attenuation correction.

Data Analysis

Scintigraphic images were analyzed by 2 experienced observers in consensus. Data from the gated stress and rest SPECT studies of all patients were analyzed using Quantitative Gated SPECT and Quantitative Perfusion SPECT softwares (QGS, QPS, Cedars Sinai Medical center, Los Angeles, CA, USA). QGS software automatically fits the left ventricular volume curve with a fourth-order harmonic function and by using the volume curve and its differential curve. ejection fraction rate (EF), the End-diastolic and end-systolic volumes (EDV, ESV) of the LV were calculated automatically by using QGS software. Transient ischemic dilation (TID) ratios were also derived from the nongated images using QPS software.

Cardiac catheterization

Coronary angiograms of the study population were performed the cardiac catheterization laboratory in the cardiology department of our hospital, and the reports of the angiograms were derived from the files of the patients. In our hospital, the routine coronary angiogram was performed with a femoral approach using the Judkins technique without using nitroglycerin, adenosine or a calcium channel blocker. All patients in the study population underwent elective coronary artery angiography using Siemens Axiom Artis DFC (Siemens Medical Solutions, Erlangen, Germany) following appropriate patient preparation. All angiograms were judged with regard to smooth appearance, luminal wall irregularities, epicardial local or diffuse caliber reduction and stenosis. Coronary arteries were classified as normal on the basis of visual assessment of the absence of any luminal irregularities.

Statistical Analysis

Descriptive statistics were expressed as mean ± SD, median (min-max) and proportions. Continuous variables are expressed as mean ± SD. Mann-Whitney-U test was used for non-parametric comparisons. Statistical analyses were performed with using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Scintigraphic and angiographic results of the study population were given in the table 1. No atheromatous plaque was detected in the coronary angiograms of the 7 patients (%26). None of the patients in this group have percutaneous transluminal coronary angioplasty (PTCA) stenting or by-pass surgery. Atheromatous plaques which caused less than 50% stenosis in the coronary arteries were reported in 4 patients (15%). Only one patient in this group had PTCA stenting and by-pass surgery. Atheromatous plaques which caused more than 50% stenosis in one coronary artery were reported in 4 patients (15%). Only one patient in this group also had PTCA stenting and by-pass surgery. Atheromatous plaques which caused more than 50% stenosis in two coronary arteries were reported in 5 patients (18%). 3 patients in this group had PTCA stenting and in addition to them, one had by-pass surgery. Atheromatous plaques which caused more than 50% stenosis in three or more coronary arteries were reported in 7 patients (26%). All patients in this group had by-pass surgery or PTCA stenting and 2 of them had both. SSS values were 4 or less in patients with normal or near normal coronary angiograms and SSS values were 5 or more in other patients of the study population. gMPI results are summarized in the table 2.

Functional parameters of the left ventricle were also compared between the groups of patients with and without normal or near normal coronary angiograms and the results were summarized in the table 3.

Table 1. Scintigraphic and angiographic results of the study population

		Angiography				Scintigraphy			
No	Age	LMCA	LAD	Cfx	RCA	TID	EDV	ESV	EF
1	55	N	N	N	N	1.47	70	19	73
2	60	N	N	N	N	1.3	121	77	37
3	62	N	N	N	N	1.15	179	102	43
4	71	N	N	N	N	1.2	182	108	41
5	60	N	N	N	N	1.3	121	77	37
6	76	N	N	N	N	1.2	65	37	43
7	70	N	N	N	N	1.23	84	32	62
8	73		%30			1.03	90	36	60
9	44		plaque			1.26	140	58	57
10	48	%30	%30			1.07	127	64	57
11	75		%40	%30		1.48	95	40	58
12	46	%30	%90			1.29	107	50	53
13	60		%50			1.28	92	49	46
14	78		%90			1.28	114	58	49
15	60		%60	plaque	diminutive	1.27	64	23	63
16	65	%25	%25	%50	%75	1.15	110	42	62
17	74		O		O	1.13	110	70	30
18	76		%50		%50	1.15	67	37	46
19	46		%80	%90		1.2	91	32	64
20	66		O		%90	1.27	86	36	57
21	62		%80	%90	O	1.2	82	40	51
22	69		O	%90	%70	1.18	80	37	54
23	78		%70	%90	%80	1.31	73	47	35
24	77		%70	om1-O	PDA-O	1.08	66	53	20
25	73	%75	%75	%75	%75	1.2	175	84	52
26	49		O	%50	O	1.1	203	124	39
27	62		%80	%95	%50	1.29	81	34	58

LMCA: Left main coronary artery, LAD: Left anterior descending artery, Cfx: Circumflex coronary artery, RCA: Right coronary artery, TID: Transient ischemic dilatation, EDV: End-diastolic volume, ESV: End-systolic volume, EF: Ejection fraction, O: Occluded, OM: Obtuse marginalis, PDA: Posterior descending artery, N: Normal

Table 2. gMPI results of the patients according to coronary angiography results

Angiography			gMPI				A/E
			TID	EDV	ESV	EF	
Group 1	Normal		1.26±0.1	117.42±48.5	64.57±35.3	48±13.9	3/4
	<50% in one or more vessels		1.21±0.2	113±24.3	49.5±13.6	58±1.4	2/2
	One vessel		1.28	94.25±22.2	45±15.2	52.75±7.4	2/2
Group 2	≥50%	Two vessels	1.18±0.1	94.5±20.4	45.25±17	50.5±15.8	2/3
		>Two vessels	1.19±0.1	121.4±62.8	67±37.3	44±15	1/6

TID: Transient isheamic dilatation, EDV: End-diastolic volume, ESV: End –systolic volume, EF: Ejection fraction, A: Adenosine/Exercise ratio

Table 3. Results of the statistical analysis of functional parameters of the left ventricle compared between two groups

	TID	EDV	ESV	EF
Group 1	1.21±0.14	115.82±39.91	59.09±29.37	51.63±11.92
Group 2	1.16±0.7	104.77±41.58	53.53±26.74	48.69±12.97
p	0.257	0.310	0.706	0.885

Group1: Patients with normal or near normal (<50%) coronary angiograms
Group2: Patients with abnormal coronary (≥50%) angiograms

Discussion

We have correlated the angiographic results with scintigraphic findings of the patients with positive TID on their gMPI scans. Our results showed that TID can be positive in patients with established coronary artery disease as well as in patients with normal coronary artery angiograms.

The increase in left ventricular volume on stress gated SPECT images according to rest SPECT images is called transient ischemic dilatation. Although, TID is probably related to a combination of myocardial ischemia which causes the stunning of the myocardium of the left ventricle (12), the exact mechanism remains unclear. When multiple coronary arteries are affected to an equivalent degree, the perfusion defects may be generally uniform in severity throughout the myocardium on stress gMPI scans which is called “balanced” ischemia. Since, radiotracer uptake in the myocardium of the LV will also be uniform in balanced ischemia, gMPI can sometimes produce false-negative results in these patient population (13). For this reason, incorporation of TID into the screening protocols may decrease false-negative results and provide additional information for severe CAD (14). As in our study group, TID values were higher than 1.1 in all patients with coronary artery disease of one or more vessels. According to our results, TID seems to be helpful for the diagnosis of balanced ischemia or extensive coronary artery disease, especially when this parameter is combined with other functional and perfusion parameters of the left ventricle. Especially, the presence of TID in patients with abnormal myocardial perfusion abnormality has already been shown to be associated with extensive coronary artery disease (15) and our results were consistent with the findings of this study.

In our study, 11 patients had normal or near normal coronary angiograms and normal myocardial perfusion SPECT images on their scans but at the same time TID values were higher than the 1,04. Although the exact significance of quantitatively elevated TID in patients with normal or minimal perfusion abnormality remains unclear and some studies showed that TID had a low prevalence and poor predictive value in the otherwise normal MPI (16). However, different scanning protocols may have different normal limits for TID ratios (17), and the lone positive TID finding can be misleading parameter during reporting the gMPI scan. It has been reported that, in studies using technetium, the sensitivity ranged from 34% to 56%, while the specificity ranged from 77% to 98% for detection of severe CAD (18).

In patients with classical syndrome X, magnetic resonance spectroscopy has been reported to reveal subendocardial hypoperfusion following intravenous administration of adenosine, implying another possible pathologic mechanism for apparent TID without extensive coronary atherosclerosis (19). In our study population, pharmacological exercise with adenosine was given to 5 of 11 patients with normal or near normal coronary angiograms and TID was a positive finding on their gMPI scans. Therefore, it is likely that in some patients, TID can be simply physiologic which it can occur as a normal variant for reasons that are not yet understood. Besides, ischemic LV dilatation with normal myocardial perfusion but without significant epicardial coronary artery disease may be present in patients with hypertrophic cardiomyopathy and with hypertensive heart disease and left ventricular hypertrophy (9, 10).

According to the description of the TID, the values of stress and rest volume ratio is more than 1 is called TID but in the literature the ratio above which TID is diagnosed ranges from 1.13 to 1.31, for studies using technetium (18). In our study population, only two patients’ TID values (7%) were less than 1.1. It has been reported in a meta-analysis that using TID ratio cutoff had little effect on specificity while, higher TID ratios resulted in decreased sensitivity (18). Therefore the diagnostic accuracy of TID to indicate the extensive coronary artery disease is still not clear and the optimal threshold for its definition should be defined.

Although, according to prior studies, TID results from subendocardial ischemia with apparent LV dilatation due to decrease in the radiotracer uptake in the endocardium (7), TID may be a manifestation of LV dilatation post-stress due to ventricular dysfunction (20). According to our results, both proposed underlying mechanisms seem to be in charge, because TID was detected in both pharmacological and treadmill exercise given patients with normal or near normal coronary angiograms, favoring lower sensitivity for indicating the existence of severe CAD. Although, overall sensitivity and specificity were reported to be similar for both exercise and pharmacologic technetium studies (17), in another study, it has been found that exercise stress resulted in a trend toward higher sensitivity than pharmacologic stress, while specificity was similar (18). Although, TID in myocardial perfusion imaging has been proposed as a high risk marker for stress induced myocardial ischemia, there is variability in the literature on its utility especially in the range of different ratios above which TID is diagnosed (18). Therefore certain thresholds for different techniques and pharmaceuticals seem to be necessary to be defined.

As a limitation of the study, the study population was not large enough to get definite conclusions.

Conclusion

In this study, we concluded that TID should be considered a high risk marker that may guide clinical management in patients with suspected or known coronary artery disease but, at the same time, it can be also positive in patients with normal coronary angiograms such as hypertensive heart disease and hypertrophic cardiomyopathy. Therefore, TID should be correlated with other perfusion and functional parameters of the left ventricle to reach the final diagnosis and if it is only finding without perfusion defects or dysfunctional parameters, it is reasonable to be cautious to interpret the gMPI scan.

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Conflict of Interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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