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Aortic Stiffness Index and Aortic Distensibility Measured by Echocardiography May Help to Improve the Equivocal Results of Myocardial Perfusion Scintigraphy

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Abstract

Objectives: Myocardial perfusion scintigraphy (MPS) is a well-established method for diagnosing coronary artery disease and risk stratification of individuals with chest pain. However, while MPS has high sensitivity and specificity for the detection of significant coronary artery disease, it has some drawbacks due to several technical difficulties. We suggest that aortic stiffness indexes measured by echocardiography, which is a well-known marker of atherosclerotic burden, may improve the equivocal test results obtained in MPS.

Materials and Methods: We prospectively enrolled 149 consecutive patients between the ages of 18 and 65 years without any previous cardiovascular disease with suspected coronary artery disease, who had undergone both SPECT MPS using Technetium-99m-sestamibi (^{99m}Tc MIBI) and transthoracic echocardiography between November 2013

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Abstract

and June 2014. Subjects were divided into three categories according to MPS results as normal, equivocal and ischemic groups.

Results: Aortic stiffness index (ASI) and aortic distensibility (AD) of the normal and equivocal groups were similar, and the ischemic group had higher ASI values compared to the normal and equivocal groups. The equivocal group had statistically lower ASI and higher AD values compared to the ischemia group (p <0.001 and <0.001). Optimal threshold cut off point for ASI to differentiate normal MPS result from MPS with ischemia in any LV wall was calculated by ROC analysis. ASI value of 3.05 was found to be cut-off value with 98% sensitivity and 87% specificity to detect ischemia (AUC=0.953 with 95% CI: 0.906 to 0.981 and p <0,001). If ASI value of >3.05 was accepted as abnormal, the frequency of abnormal ASI in the normal, equivocal, and ischemia groups were 11%, 19%, and 98%, respectively. The equivocal group had similar number of patients with abnormal ASI compared to the normal group (p=0.262) while it had statistically a lower number of patients with abnormal ASI than the ischemia group (p<0.001)

Conclusion: However, aortic stiffness and aortic AD indexes alone cannot diagnose coronary artery disease (CAD), but may help to discriminate patients with CAD from those without CAD whose MPS results are equivocal.

Keywords: Aortic stiffness indexes, echocardiography, myocardial perfusion scintigraphy

Introduction

Myocardial perfusion scintigraphy (MPS) is a well-established method for the investigation in the differential diagnosis of new-onset chest pain as well as the management of patients with known coronary heart disease (CAD). It is a very valuable diagnostic tool especially for the patients with basal electrocardiography (ECG) changes [such as left bundle branch block (LBBB), left ventricle (LV) hypertrophy, pre-excitation] and with non-diagnostic exercise ECG test results, and for people unable to perform exercise ECG test due to their orthopedic or neurological problems[1].

The sensitivity and specificity of single photon emission computed tomography (SPECT) MPS test for the diagnosis of a significant coronary lesion (defined as coronary stenosis of more than 50%) were 86% and 74%, respectively[2]. A false negative result can be obtained with the SPECT MPS due to some causes such as balanced multiple vessel diseases. Thus, approximately 13-15% of patients with left main disease can have normal perfusion scintigraphy owing to balanced ischemia in multivessel CAD[3,4]. Another pitfall in MPS is equivocal results due to attenuation artifacts, patient motion during the test, or incorrectly performed technical analysis. For example, an elevated diaphragm can cause an obvious fixed defect in the inferior wall in men, and breast artifact can result in an obvious defect in the anterior wall in women. The presence of LBBB is another pitfall in MPS results. Especially in the evaluation of anterior and septal wall, it can be a source of ambiguous outcomes. Also incorrectly performed technical analyses such as multidetector misalignment, incorrectly designed bull's eye reconstruction, and the presence of non-uniform flood fields can lead to false positive or equivocal results[5]. These results can lead to an increase in the number of invasive diagnostic applications, and finally can cause socio-economic and psychological burden for the patients. In such false positive cases, applying gated studies, attenuation correction algorithm, and prone imaging technique can improve diagnostic accuracy but cannot solve the problem[6-8].

In this respect, echocardiographic findings which measure aortic elasticity and systolic and diastolic functions of the LV may help to improve the diagnostic accuracy of SPECT MPS since reliability and reproducibility of these

measurements have been well-established in evaluating cardiovascular risk. The arterial stiffness develops with increasing age and diseases such as hypertension, diabetes mellitus, atherosclerosis, and chronic kidney disease[9]. So, it reflects the cardiovascular burden of the relevant subject. In the studies dealing with arterial stiffness, pulse wave velocity (PWV) technique has been used extensively, but echocardiography has not been used effectively to measure arterial stiffness[10-12]. It is a very valuable tool in this aspect since it measures central arterial rather than peripheral arterial stiffness, which has better correlation with cardiovascular outcome[13].

This study aimed to examine the role of aortic elasticity in further evaluation of different MPS results (normal scan, equivocal, and ischemia) among patients with suspected CAD.

Materials and Methods

Subjects

We prospectively studied 149 consecutive patients with suspected CAD, who had undergone both SPECT MPS using Technetium-99m-sestamibi (^{99m}Tc MIBI) and transthoracic echocardiography between November 2013 and June 2014. Subjects between the ages of 40 and 65 years were enrolled in the study. Patients with previously diagnosed CAD, a history of acute coronary syndrome or peripheric vascular disease, chronic kidney disease (creatinine >1.4 mg/dL), advanced liver disease (transaminase levels more than three times of the upper limit), a history of previous stroke, any cancer, acute infection at the time of the test, hyper- or hypothyroidism, symptomatic congestive heart failure (NYHA functional capacity class III or IV), LV ejection fraction less than 50%, and any congenital heart disease were excluded. Additionally, patients with a history of myocardial infarction based on echocardiography and ECG findings were also ruled out.

The following data were also obtained: age, gender, height, weight, and the presence of cardiovascular risk factors. Cardiovascular risk factors were determined according to the following criteria: positive family history for CAD (the presence of CAD in first-degree family members, male at the age of <55 years and/or female at the age of <65 years), cigarette smoking (current smoking or smoking in the last 2 years), hypertension (the last three blood pressure measurements >140/90 mmHg or treatment with antihypertensive medication within the last six months), and hyperlipidemia (current usage of cholesterol-lowering medication). Laboratory findings such as serum levels of high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol, triglyceride (TG), creatinine, thyroid stimulating hormone (TSH), and fasting blood glucose were also measured for all patients. Body mass index (BMI) was defined according to the World Health Organization criteria. Patients were classified as normal weight (BMI=18.5-24.9 kg/m^2), overweight (BMI=25.0-29.9 kg/m^2), obese class I (BMI=30.0-34.9 kg/m^2), obese class II (BMI=35.0-39.9 kg/m^2), and obese class III (BMI=40 kg/m^2 or more). The ethical approval was provided for the study from Bozok University Local Ethical Committee (approval date and no: 24.02.2014/12) and informed consent from each patient for the study and the investigation were obtained in accordance with the principles outlined in the Declaration of Helsinki.

Myocardial Perfusion Scintigraphy Protocol

The SPECT data were acquired with the Gated technique using the double-head SPECT γ-camera system (Philips Medical Systems Brightview Gamma Diagnostics, Holland) equipped with a high-resolution, low-energy collimator. A total of 32 projections (35 projection/s) were obtained over a 180° circular orbit, at the 20% energy window which centered 140 keV for gamma emission of ^{99m}Tc. Myocardial images were projected into tomographic slices in the short axis, long vertical axis, and horizontal-long axis views. 4D-M SPECT software was used for semiquantitative analysis of data. The SPECT images were reconstructed by filtered back projection method using a Butterworth filter (order 5; cut-off frequency 0.50).

The subjects were undergone either exercise treadmill test with modified Bruce protocol (TMT) or, when contraindications to exercise were present, vasodilatory stress with intravenous adenosine using a standard infusion rate of 140 µg/kg per minute. Target level to evaluate the TMT to search for the presence of ischemia was defined as at least 6-minute exercise and achieving at least 85% of target heart rate which equals to 220 minus age in years. Injection of the radiopharmaceutical was performed at peak exercise, or in the third minute of pharmacological stress induction.

The perfusion images were evaluated independently by two experienced nuclear medicine physicians without clinical data. The disagreement was solved by consensus. The myocardium was divided into 17 segments for semiquantitative analysis by following the American Society of Nuclear Cardiology, the American College of Cardiology, and the American Heart Association Guidelines[14]. A scale of 0-4 was used for grading wall motion: (0: Normal, 1: Mildly hypokinetic, 2: Hypokinetic, 3: Akinetic, and 4: Dyskinetic) by automatic scores for each of the segments[15]. An abnormal motion was defined as a score of >2. According to the test results patients were classified into three groups. The normal group included the patients with normal Gated SPECT MPS scans. The equivocal group included indeterminate scan results that patients with slight perfusion and mildly hypokinetic wall motion had. The third group was the ischemia group including patients with apparent abnormal perfusion and wall motion findings in any segment of LV myocardium at stress.

Echocardiography Protocol

Two-dimensional, M-mode, pulsed wave Doppler, and Tissue Doppler echocardiography were performed on an ultrasound machine (Presound alpha 7, IPF 1701 Model, 2009; Hitachi Aloka Medical, Ltd. Tokyo, Japan) with a 2.5-MHz transducer by a cardiologist blinded to the study before performing MPS. Standard 2-dimensional measurements (LV diastolic and systolic dimension, ventricular septum and posterior wall thickness, left atrial diameter, LV ejection fraction) were obtained as recommended by the American Society of Echocardiography[16]. The mitral inflow velocities were traced, and peak velocity of early diastolic mitral inflow (E) and late diastolic mitral inflow (A) was obtained. Mitral annular velocities were obtained by Doppler tissue imaging using the pulsed-wave mode. Early diastolic mitral annular (Em), late diastolic (Am) and systolic velocities (Sm) of the mitral annulus were measured from the apical 4-chamber view with a 2- to 5-mm sample volume placed at the lateral edge of the mitral annulus. All measurements were carried out during expirium. Normal diastolic function (DD) was defined as E/A ratio >1, Em >8 cm/s, Em/Am >1 and E/Em <8. Grade I DD was defined as E/A ratio <1, Em <8 cm/s, Em/Am <1, and E/Em <8. Grade II DD was defined as E/A ratio >1 and <2, Em <8 cm/s, Em/Am <1 and E/Em between 8 and 15; Grade III DD was defined as E/A ratio >2, Em <8 cm/s and E/Em >15.

The blood pressure (BP) levels were measured from the right and left arms of the subjects in a sitting position by a trained observer blind to the study in the echocardiography laboratory. BP was measured twice at five-minute intervals. The systolic BP (SBP) and diastolic BP (DBP) were recorded at the first and fifth Korotkoff phases, respectively, using a mercury sphygmomanometer. The average of the four BP measurements was used for analysis. The difference of SBP and DBP was used as pulse pressure (PP).

Following the echocardiographic examination of heart, at parasternal long axis M-mode images, the systolic (Asd) and diastolic (Add) aortic diameters of ascending aorta from lower margin of upper wall to upper margin of lower wall were measured at 3 cm distal to the aortic valve level, discriminating diastole and systole by using simultaneous ECG recordings. Average heart rates at examination were statistically similar ($p>0.05$) among the normal, equivocal and ischemia groups (73±5, 72±3, and 74±6 bpm, respectively). While aortic stiffness index was calculated by using ASI= ln (SBP/DBP)/[(Asd-Add)/

Add] formula, aortic distensibility was obtained by using AD [1/(10³xmmHg)]=2x [(Asd-Add)/Add]/PP formula[17].

Statistical Analysis

Statistical analyses were performed using the SPSS software version 18. Continuous variables are presented as mean ± SD, and categorical variables are presented as frequencies (%). Kolmogorov-Smirnov test was used to analyze variables' distribution patterns. Hemoglobin, creatinine, total cholesterol, and LDL were normally distributed while all other continuous variables were not normally distributed. Categorical variables were compared using the chi-square test. Spearman simple correlation analyses were performed to determine the association between continuous parameters accordingly while Mann-Whitney U test and Kruskal-Wallis were used to compare groups accordingly. A p value of less than 0.05 was considered to show statistically significant result. To find diagnostic cut-off value of aortic stiffness index for the differentiation of patients with normal scan from patients with ischemia, a receiver operating characteristic (ROC) curve analysis was constructed, and the area under the curve (AUC) was reported, which is considered to be representative of the discriminative ability of the variable cut-off. Sensitivity and specificity values of the best cut-off variables were determined using ROC curve analysis. The cut-off levels of aortic stiffness index were calculated using MedCalc software package.

Results

Between November 2013 and June 2014, one hundred and eighty-one patients were referred to MPS, 32 of them were excluded from the study according to exclusion criteria described previously. The remaining 149 patients were eligible for the analysis. Of 149 patients, 51 (34%) adequately succeeded an exercise TMT while remaining 98 patients (66%) underwent vasodilatory stress with intravenous adenosine.

ECG recordings of the subjects in normal and equivocal groups were normal during the treadmill ECG part of MPS protocol in respect to coronary ischemia. Distribution of type of stress test among the groups was statistically non-significant (p>0.05). The normal group was composed of 55 patients, the equivocal group included 54 patients, and the ischemia group had 40 patients according to MPS results. In the equivocal group, eight patients (15%) had equivocal scan result at the inferior wall, 15 patients (28%) at the inferolateral wall, 20 patients (37%) at the anterior wall, eight patients (15%) at the anterolateral wall, and three patients (5%) at the apical part of the LV.

Subjects in the equivocal group were further evaluated in suspect of CAD accordingly. We found that 29 patients had normal coronary arteries according to the results of conventional coronary angiography (CAG) and 20 patients had zero-score coronary computed tomographic angiography results, five patients had non-obstructive CAD upon CAG or computed tomography examinations.

In the ischemia group, 10 patients (25%) had apparent abnormal perfusion and/or wall motion findings at the inferior wall, 13 patients (32%) at the inferolateral wall, seven patients (18%) at the anterior wall, four patients (10%) at the anterolateral wall, and six patients (15%) at the apical part of the LV. Further evaluation of the subjects revealed that 93% of subjects with ischemia on MPS (n=37) revealed obstructive CAD according to the CAG results. Three subjects had non-obstructive CAD, and one subject had normal CAG.

Baseline characteristics of the patients in respect to groups were shown in Table 1. Average ages of the groups, as well as gender distribution, were similar to each other. The presence of cardiovascular risk factors among the groups was also statistically similar.

Laboratory findings of the groups were expressed in Table 2. Although creatinine and TG levels of the ischemia group were higher than those of other groups, it did not reach the level of significance (p values 0.064 and 0.092, respectively), and also HDL level of the ischemia group was lower without statistical significance (p=0.081).

In echocardiographic examination, we found that the equivocal group had similar left ventricular ejection fraction compared to the normal group (p=0.856) and

the ischemia group (p=0.288). Similarly, IVSd and PWd measurements of the equivocal group did not differ from those of the normal group (p values: 0.172 and 0.275, respectively) and the ischemia group (p values: 0.056 and 0.076, respectively). In respect to diastolic function, the equivocal group had statistically similar mitral E/A and mitral anulus Em/Am ratio compared to the normal group (p values: 0.174 and 0.96 accordingly) while it had higher mitral E/A and mitral anulus Em/Am ratios than those of the ischemia group (p values <0.001 for both). Similary, number of patients with diastolic dysfunction grade I and above was statistically similar between the equivocal and normal groups (p=0.287) while the ischemia group had higher number of patients with diastolic dysfunction of any grade compared to the equivocal group (p<0.001). Table 3 summarized echocardiographic findings of the groups.

Average ASI values were 2.61±0.48 for the normal group, 2.60±0.49 for the equivocal group, and 3.80±0.38 for the ischemia group (Table 4). The equivocal group had statistically similar ASI and AD values in comparison to the normal group (p values: 0.505 and 0.694) while the equivocal group had statistically lower ASI and higher AD values compared to the ischemia group (p values

Table 1. Clinical and demographic data of the groups

	Normal Group (n=55)	Equivocal Group (n=54)	Ischemia Group (n=40)	p
Age	56±11	55±11	56±9	0.596
Gender (F/M)	35/20 (64/36)	32/22 (59/41)	20/16 (60/40)	0.884
Height (cm)	161±7	164±5	163±6	0.023
Weight (kg)	76±12	81±14	84±9	0.018
BMI	30±5	30±6	31±4	0.154
DM, n (%)	16 (29)	12 (22)	11 (27)	0.669
HT, n (%)	30 (54)	27 (50)	18 (45)	0.654
Cigarette smoking, n (%)	9 (16)	10 (19)	9 (22)	0.750
Family history of premature CAD, n (%)	8 (14)	4 (7)	4 (10)	0.483
Hyperlipidemia, n (%)	8 (14)	4 (7)	6 (15)	0.404
SBP (mmHg)	124±15	124±10	132±13	0.001
DBP (mmHg)	78±6	79±5	78±6	0.200

BMI: Body mass index, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, F: Female, M: Male

Table 2. Laboratory findings of the groups

	Normal Group (n=55)	Equivocçal Group (n=54)	Ischemia Group (n=40)	p
Hemoglobin (g/dL)	13.3±1.4	13.7±1.4	13.8±1.7	0.168
FBG (mg/dL)	113±41	116±46	128±53	0.597
Cr (mg/dL)	0.81±0.17	0.80±0.15	0.87±0.16	0.064
TC (mg/dL)	201±38	196±28	209±46	0.261
TG (mg/dL)	163±81	151±54	197±98	0.092
HDL (mg/dL)	45±10	45±9	41±7	0.081
LDL (mg/dL)	123±33	122±24	126±31	0.793
ALT (IU/L)	19±12	21±12	17±8	0.555
AST (IU/L)	19±9	20±10	17±5	0.161
TSH (µIU/mL)	1.75±1.14	1.67±1.25	1.48±0.91	0.639

FBG: Fasting blood glucose, Cr: Creatinine, TC: Total cholesterol, TG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein, ALT: Alanine transaminase, AST: Aspartate transaminase, TSH: Thyroid sitimulating hormone

<0.001 and <0.001). Optimal threshold cut-off point for ASI to differentiate normal MPS result from MPS with ischemia in any LV wall was calculated by ROC analysis. ASI value of 3.05 was found to be cut-off value with 98% sensitivity and 87% specificity to detect ischemia (AUC=0.953 with 95% CI=0.906 to 0.981 and p value <0.001). If ASI value of >3.05 was accepted as abnormal, frequency of abnormal ASI in the normal, equivocal, and ischemia groups were 11%, 19%, and 98%, respectively. The equivocal group had similar number of patients with abnormal ASI compared to the normal group (p=0.262) while it had statistically lower number of patients with abnormal ASI than the ischemia group (p<0.001)

Discussion

In this study, we have found that patients with equivocal SPECT MPS result had similar aortic elastic properties and diastolic functions compared to patients with normal scan while they had better aortic elasticity and less diastolic dysfunction frequency compared to SPECT MPS result with ischemia in any segment of LV walls.

CAD causes significant mortality and morbidity if left undiagnosed and untreated, and it is multifactorial with genetic and environmental background[18]. Cardiovascular risk factors, such as hypertension, diabetes, smoking cigarette, and obesity, all make the picture more complex to be understood. Thus, clinician needs tools with high sensitivity and specificity for prompt diagnosis. In this aspect, SPECT MPS gives an ample solution for such need with sensitivity and specificity of 86% and 74%, respectively[2], but still it has some limitations like attenuation defects, and normal scan result in three-vessel or left main CAD. Thus, we proposed measurement of aortic elasticity for better differentiation of these false negative and false positive results.

The type of radiopharmaceuticals used for MPS can change the ability to diagnose significant CAD. Thalium with low-energy X-ray emission and redistribution

Table 3. Echocardiographic examination results of the groups

	Normal Group (n=55)	Equivocal Group (n=54)	Ischemia Group (n=40)
LVEF (%)	63±3	63±4	62±3
IVSd (mm)	10±1	10±1	11±1
PWd (mm)	10±1	10±1	11±1
LA diameter (mm)	39±4	39±3	41±3
Mitral E/A ratio	1.15±0.52	1.24±0.42	0.76±0.16
Mitral anulus TDI Em/Am	1.16±0.60	1.37±0.59	0.69±0.27
Diastolic Function Normal (%)	27 (49)	32 (59)	6 (15)
Grade I DD (%)	26 (47)	18 (33)	34 (85)
Grade II DD (%)	2 (4)	4 (8)	0 (0)
Grade III DD (%)	0 (0)	0 (0)	0 (0)

LVEF: Left ventricle ejection fraction, IVSd: Interventricular septum diastolic thickness, PWd: Posterior wall diastolic thickness, LA: left atrium, TDI: Tissue Doppler imaging, DD: Diastolic dysfunction, E: Early, A: Late

Table 4. Aortic elasticity parameters of the groups

	Normal Group (n=55)	Equivocal Group (n=54)	Ischemia Group (n=40)	p
ASI	2.61±0.48	2.60±0.49	3.80±0.38	0.000
AD [1/(10^3xmmHg)]	5.98±3.05	5.96±2.75	1.59±0.98	0.000
Abnormal ASI (%)	6 (11)	10 (19)	39 (98)	

ASI: Aortic stiffness index, AD: Aortic distensibility
ASI value of 3.05 was used as a cut-off value with 98% sensitivity and 87% specificity to detect ischemia (AUC=0.953 with 95% CI: 0.906 to 0.981 and p value <0,001). ASI value of >3.05 was accepted as abnormal

capability has low and non-reproducible image quality compared to technetium-based compounds[19]. Thus, we evaluated our patients with technetium-based compounds in this study.

To reveal significant CAD, the patients undergo different stresses which can be evoked either by exercise or pharmaceutical agents (dipyridamole, adenosine, dobutamine, and regadenoson). These pharmaceutical agents are currently used in patients unable to exercise to evaluate myocardial perfusion with different diagnostic accuracy. A recent study conducted by Conti et al. showed that adenosine-based SPECT had better sensitivity and specificity than dipyridamole-based SPECT[20] while diagnostic value of adenosine-based SPECT was found to be similar compared to exercise-based SPECT[21]. We also used intravenous adenosine infusion to produce coronary vasodilatation in 66% of the study population. The rest performed exercise treadmill test to induce coronary ischemia.

Attenuation defects due to non-cardiac tissues such as breast and diaphragm can result in artifactual appearance of wall motion abnormalities in SPECT. For example, planar projection images of female patients with large breast tissue can cause artifacts of reduced-perfusion type in the anterior wall of the LV while the left hemidiaphragm can lead attenuation artifacts in the inferior wall of the LV especially among tall, asthenic male patients[5,8]. In our study, we also found that 94% of female patients with attenuation defects (n=30) had anterior wall involvement while 95% of male patients with attenuation defects (n=21) had inferior wall involvement ($p<0.001$). Apart from attenuation artifacts, there are some gray zones in the evaluation of patients with slight perfusion and mildly hypokinetic wall motion on SPECT MPS. The presence of LBBB is another pitfall in MPS results. Especially in the evaluation of anterior and septal wall, it can be a source of ambiguous outcomes. Also incorrectly performed technical analyses such as multidetector misalignment, incorrectly designed bull's eye reconstruction, and the presence of non-uniform flood fields can produce false positive or equivocal results[5].

There are few techniques offered to get rid of these equivocal test results. However, the usage of sestamibi instead of thallium, prone imaging, and gated SPECT analyses helps to differentiate real ischemia from false positive[5,8,22], but these measures are not enough all the time. Prone imaging sometimes cannot be possible for obese patients. Although gated SPECT has introduced significant solution for equivocal results especially in case of attenuation artifacts, it needs time, experience for evaluation and also availability of new hardware and software is compulsory for quick assessment[23].

In this aspect, aortic elasticity which reflects vascular stiffening can fill the important gap in the evaluation of attenuation defects. Aortic elasticity was expressed as aortic stiffness index and aortic distensibility. These parameters are inversely related and a hallmark of the aging and atherosclerosis[24]. The presence of cardiovascular risk factors enhances atherosclerotic process; therefore, reduces aortic elasticity which leads an increase in ASI and reduction in AD. Roos et al. reported in their study that vascular stiffness was related to the extent of wall motion abnormalities on MPS in asymptomatic diabetics[25]. They used the carotid-femoral PWV method to measure vascular stiffness. We used aortic indexes via echocardiography to evaluate vascular stiffness. It is known that the aorta gives better reflection of central hemodynamics than the femoral artery since the femoral artery is a muscular vessel[26,27]. The effect of atherosclerosis on muscular vessels are more attenuated than elastic great vessels such as the aorta and branches[26,27]. Moreover, the necessity of groin exposure (problematic especially in obese patients) and unknown distance between two recording sites (resulting overestimation in obese patients) are other limitations of PWV method which reduces its accuracy[27]. Echocardiographic method is free of all these limitations and easy to apply in measuring vascular stiffness.

Aortic stiffness reflects atherosclerosis. In our study, we also found that patients with ischemia on MPS had

higher ASI (3.80±0.38) compared to patients with normal MPS (2.61±0.48) (p<0.001). Both groups had similar age, gender, and frequency of cardiovascular risk factors. Similar correlation existed between the ischemia group and the equivocal group in respect to ASI (3.80±0.38 vs 2.60±0.49 with p<0.001). In the analysis, we showed that there was not any significant difference between the normal scan and equivocal groups in respect to ASI or AD (p values 0.505 and 0.694 respectively). Also, they were similar in age, gender, and the presence of cardiovascular risk factors. Also, laboratory findings such as lipid profile, fasting blood glucose, hemoglobin, and TSH levels were similar between the normal and equivocal groups. In parallel to all these findings, frequency of LV diastolic dysfunction in the equivocal group was similar to the normal group (p=0.287) and less than the ischemia group (p<0.001).

All these findings indicated that patients with equivocal test results had similar clinical characteristics in respect to the normal scan group. Thus, in case of equivocal MPS results, aortic elasticity can also be measured and can guide nuclear medicine physician since it is known that clinical data is necessary to increase diagnostic accuracy even in the interpretation of gated SPECT[5]. Roos et al. found increased vascular stiffness in asymptomatic diabetics with ischemia on MPS, but we enrolled subjects from real life with and without diabetes mellitus[25]. Both studies recruited subjects with statistically similar BMI, ratio of hypertensive patients, and cigarette smoking. However, Roos et al. did not comment on vascular stiffness of patients with equivocal test results such as attenuation artifacts since they reported that they eliminated such results by using gated SPECT[25]. Here, we included patients with equivocal test results. To remove effect of diabetes on vascular stiffness and to rule out existing vascular stiffness, subjects with diabetes or known cardiovascular disease were excluded.

Conclusion

All these measures cannot make gated SPECT a gold standard method, and we still need additional clinical parameters for correct diagnosis in case of equivocal test results. So, we assumed that aortic stiffness index and aortic distensibility, parameters measuring aortic elasticity, may improve diagnostic accuracy of SPECT, especially in case of equivocal test results.

Ethics

Ethics Committee Approval: Obtained from Bozok University Local Ethics Committee for non-invasive Scientific Searches (approval date and no: 24.02.2014/12)

Informed Consent: Informed consent from each patient for the study and the investigation were obtained in accordance with the principles outlined in the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.E., S.K., V.K.V., Y.T., S.S.G., A.R.E., Concept: H.E., S.K., V.K.V., Y.T., S.S.G., A.R.E., Design: H.E., S.K., V.K.V., Y.T., S.S.G., A.R.E., Data Collection or Processing: H.E., S.K., V.K.V., Y.T., S.S.G., A.R.E., Analysis or Interpretation: H.E., S.K., V.K.V., Y.T., S.S.G., Literature Search: H.E., S.K., V.K.V., Y.T., S.S.G., A.R.E., Writing: H.E., S.K., V.K.V., Y.T., S.S.G., A.R.E.

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