

THE ABILITY OF QUANTITATIVE DATA EVALUATED BY ^{99m}Tc-MIBI MYOCARDIAL PERFUSION SCINTIGRAPHY TO PREDICT CORONARY ARTERY DISEASE

99MTC-MIBI MİYOKARD PERFÜZYON SİNTİGRAFİSİ İLE DEĞERLENDİRİLEN KANTİTATİF VERİLERİN, KORONER ARTER HASTALIĞINI ÖNGÖRME KABİLİYETİ

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Öz

Amaç

^{99m}Tc-MIBI miyokardiyal perfüzyon görüntülemenin, visual yorumunun etkinliği, koroner arter hastalığının (KAH) tanıs ve prognostik değerlendirmesinde defalarca doğrulanmasına rağmen, bilgisayar programlarına bağımlı otomatik kantitatif değerlendirmenin etkinliği tartışma konusudur. Biz çalışmamızda, sum stress score (SSS) ve sum difference score (SDS) gibi otomatik kantitatif verileri, koroner anjiyografi sonuçları ile karşılaştırdık. SSS ve SDS değerlerinin, koroner arter hastalığını öngörme kabiliyetini araştırdık.

Gereç ve Yöntem

SSS ve SDS, myocardial perfüzyonun global skorlamasında kullanılan ölçümlerdir. SSS'u iskeminin derecesini gösterirken, SDS iskeminin geri döndürülebilir olma derecesini tanımlar. Miyokardiyal perfüzyonun global skorlamasında, SSS'u 4 ve üzerinde ise MPS pozitif olarak değerlendirildi. Koroner anjiyografide ise >%50 üzerinde darlık pozitif olarak değerlendirildi. SSS'nu hafif (4-8), orta (9-12) ve ileri (>13) düzeyde

hipoperfüzyon olmak üzere 3 gruba ayırdık. SDS'nu %10 un altı ve üstü olmak üzere 2 gruba ayırdık. Bu kantitatif verileri, 3 grup koroner anjiyografi sonuçlarıyla karşılaştırdık (<%50, %50-70, >%70 darlık).

Bulgular

Çalışmaya toplam 104 anjiyo uygulaması yapılan hasta dahil edildi. Hastaların genel kantitatif MPS ve anjiyografi yöntemleri arasındaki pozitiflik tespitindeki doğruluk %80,8 olarak hesaplandı. Uyuşum değeri anlamlı bulundu (Kappa=0,602; p<0,001). SSS grupları ile anjiyografi grupları karşılaştırıldığında, uyuşum değeri orta düzeyde fakat anlamlı bulundu (Kendall's tau-b=0,373; p=0,014). SDS grupları ile anjiyografi grupları karşılaştırıldığında, uyuşum değeri düşük düzeyde anlamlı bulundu (Kendall's tau-b=0,234; p=0,014).

Sonuç

MPS'de genel kantitatif değerlendirmenin, KAH'nı tahmin etme değeri yüksek olarak bulunmakla birlikte ayrıntılı miyokardiyal perfüzyon skorlamanın (SSS, SDS), KAH'lığını tespit oranları yeterli düzeyde değildi. Bu nedenle, ayrıntılı miyokard perfüzyon skorla-

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masının tek başına KAH tespitinde yetersiz olacağını ve tek başına kullanılmaması gerektiğini düşünüyoruz.

Anahtar Kelimeler: Miyokard Perfüzyon Sintigrafisi, SSS, SRS, SDS

Abstract

Objective

Although the efficacy of the visual interpretation of ^{99m}Tc-MIBI myocardial perfusion scintigraphy has been repeatedly confirmed in the diagnostic and prognostic evaluation of coronary artery disease (CAD), the efficacy of the automated quantitative evaluation dependent on computer programs is controversial. In our study, we compared automated quantitative data, such as the sum stress score (SSS) and the sum difference score (SDS), with coronary angiography results. We investigated the ability of SSS and SDS values to predict coronary artery disease.

Materials and Methods

SSS and SDS are measurements used in the global scoring of myocardial perfusion. While SSS indicates the degree of ischemia, SDS defines the reversibility degree of ischemia. In the global scoring of myocardial perfusion, when the SSS was 4 and above, MPS was evaluated as positive. In the coronary angiography, a stenosis value of >50% was evaluated as positive. We divided the SSS into three groups; mild (4-8), moderate (9-12), and advanced (>13) hypoper-

fusion. We divided the SDS into two groups as below and above 10%. We compared the subsequent quantitative data with the results of the three groups of coronary angiographies (<50%, 50-70%, and >70% stenosis).

Results

A total of 104 patients who underwent angiography were included in the study. The accuracy in detecting positivity between the general quantitative MPS and angiography methods of the patients was calculated as 80.8%. The agreement value was found to be significant (Kappa=0.602; p<0.001). When the SSS groups and angiography groups were compared, the agreement value was found to be moderate but significant (Kendall's tau-b=0.373; p=0.014). Comparing the SDS groups and angiography groups, the agreement value was found to be significant at a low level (Kendall's tau-b=0.234; p = 0.014).

Conclusion

Although general quantitative evaluation in MPS had a high predictive value of CAD, the CAD detection rates of detailed myocardial perfusion scoring (SSS, SDS) were not at a sufficient level. Therefore, we suggest that detailed myocardial perfusion scoring alone will be insufficient in detecting CAD, and should not be used alone.

Keywords: Myocardial Perfusion Scintigraphy, SSS, SRS, SDS

Introduction

In patients with pre-diagnosed coronary artery disease (CAD), it is important to confirm the diagnosis and estimate the risk of cardiac events to determine an optimal treatment strategy. In the guidelines on the assessment of cardiovascular risk by the American College of Cardiology / American Heart Association (ACC/AHA), the importance of age, gender, diabetes mellitus (DM), blood pressure, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and smoking has been emphasized (1).

Patients with symptoms of CAD, or at risk of cardiac events, can be evaluated by diagnostic Myocardial Perfusion Scintigraphy (MPS). The Single-Photon Emission Computed Tomography (SPECT) Gamma Camera is an imaging method that enables the evaluation of myocardial perfusion as well as other scintigraphy examinations. Depending on the type of myocardial perfusion disorder, MPS may reveal scar-

ring after myocardial infarct (MI), reversible perfusion deficiency (ischemia) during stress examination, and ischemia surrounding scarring after MI (peri-infarct ischemia) (2). MPS can be interpreted visually or quantitatively in an automated manner. The effectiveness of visual interpretation in the diagnostic and prognostic evaluation of CAD has been confirmed in many studies (3).

In the quantitative evaluation using computer software, the scintigraphic images obtained from the patient are compared with a database containing average data from healthy individuals. Unlike the visual assessment, a 17-segment polar map corresponding to the left ventricular walls is used. This polar map is used to calculate the perfusion score by considering both the severity and extent of the perfusion disorder (4). In the global scoring of myocardial perfusion, metrics such as the sum stress score (SSS), sum rest score (SRS), and sum difference score (SDS) are used. In the polar map obtained from both stress

and rest evaluation, SSS indicates the degree of ischemia, while SDS indicates the reversibility degree of ischemia (5).

Although the efficacy of the visual interpretation of ^{99m}Tc -MIBI SPECT Myocardial perfusion scintigraphy has been repeatedly confirmed in the diagnostic and prognostic evaluation of coronary artery disease, the efficacy of the automated quantitative evaluation dependent on computer programs is controversial. In this study, we compared automated quantitative data (SSS and SDS) with the results of coronary angiography. We investigated the ability of SSS and SDS values to predict coronary artery disease.

Materials and Methods

Subjects

104 patients who underwent ^{99m}Tc -MIBI MPS between 2019-2020 for suspected CAD or risk of cardiac events, and who had undergone coronary angiography within 1 month were included in the study. Patients with a history of bypass or stents before MPS were excluded from the study. In addition, patients who could not exhibit an effort in the stress test and who underwent pharmacological stress were excluded from the study. The study was approved by the Suleyman Demirel University Ethics Committee (approval number: 1, date: 08.01.2021).

^{99m}Tc -MIBI MPS Protocol

Patients were called for imaging during fasting. A double day protocol was applied, with stress on the 1st day (during effort), and rest on the 2nd day (dur-

ing resting). In the stress test, patients were taken on the treadmill and when they had reached 85% effort capacity, 20-30mCi (740-1110 MBq) ^{99m}Tc -MIBI was applied intravenously. Images were obtained 30 minutes after the injection by using a low-energy, high-resolution parallel hole collimator with a double-headed SPECT Gamma Camera (Siemens Symbia Evo Excel; Siemens, Hoffmann Estates, IL 60192, USA). In the rest study, while patients were at rest, 20-30mCi (740-1110 MBq) ^{99m}Tc -MIBI was applied intravenously and the images were obtained with the same device 60 minutes after the injection.

Polar Map and Image Analysis

Without making a visual evaluation of the images, an automated quantitative evaluation process was initiated. The 17-segment polar map created by the American Heart Association (AHA) was used for the quantitative evaluation. The polar map presents a 3-dimensional tomographic image of left ventricular perfusion as a 2-dimensional map. The outermost segments correspond to the basal segments of the left ventricular walls, and the midmost segment (segment 17) represents the cardiac apex (Figure 1).

The polar map offered automatically by the computer scores each segment from 0 to 4 according to the degree of perfusion. While 0 points indicate normal perfusion, 1 point indicates mild hypoperfusion, and 4 points indicates the absence of perfusion. This polar map is used to calculate the perfusion score by considering both the severity and extent of the perfusion disorder. The sum stress score (SSS), sum rest score (SRS), and sum difference score (SDS) are meas-

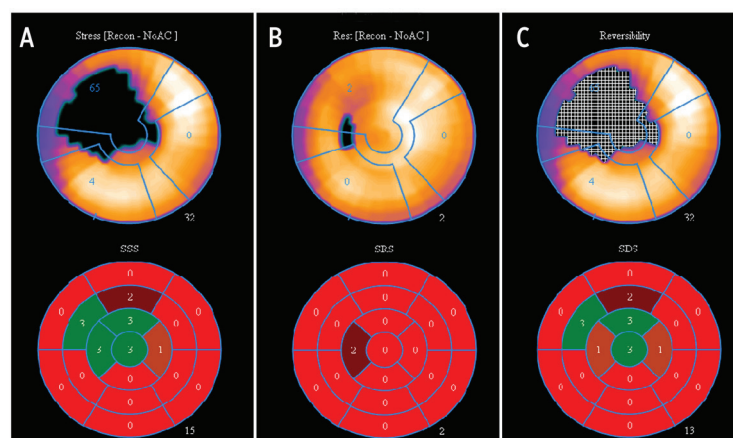


Figure 1

The figure presents the extent of a stress perfusion deficit. The perfusion deficit involves the apex, anterior and anteroseptal wall, the ischemic area may correspond to the left anterior descending artery branches. The polar map divided into 17 segments. A) Sum Stress Scores (in this case amounting to 15 points) B) Sum Rest Scores (2 points) C) Sum Difference Scores (13 points).

urements used in global scoring of myocardial perfusion. SSS shows the extent and severity of perfusion defects in the polar map obtained in the stress study. The stress score is obtained with 17 segments and scoring is between 0-4 for each segment.

An SSS score lower than 4 indicates normal perfusion (no significant perfusion disturbances), a score between 4-8 indicates slightly abnormal perfusion, a score between 9-12 indicates moderately abnormal perfusion, and a score of 13 or above indicates the presence of significant ischemia. SRS shows the extent and severity of perfusion defects in the polar map obtained in the rest study. SDS gives the difference in perfusion defect between stress and rest studies. SDS is used to describe the extent of reversibility of ischemia. Many studies have shown that patients with an SDS over 10% benefit from revascularization (6).

In the quantitative general evaluation of MPS in our study, when the SSS was 4 and above, MPS was evaluated as positive in the global scoring of myocardial perfusion. In the coronary angiography, a stenosis value of >50% was evaluated as positive. We divided the SSS into 3 groups as mild hypoperfusion (4-8), moderate hypoperfusion (9-12), and advanced hypoperfusion (>13). Furthermore, the SDS was divided into 2 groups as below and above 10%. We compared these quantitative data with the results of coronary angiography (<50%, 50-70%, and >70% stenosis). We compared the quantitative data with patients' cardiac event risk factors (DM, HT, HL smoking, obesity, gender, age, and menopause). We also compared the perfusion defects in the localizations corresponding to the myocardial walls supplied by the left ventricular coronary arteries (LAD, RCA, CX) and the vascular results in coronary angiography shown by the polar map.

Coronary Angiography and Evaluation

It is well known that the standard procedure for examining the coronary anatomy is by coronary angiography. However, since this test is an invasive procedure, and that there may be a risk of complications, it should be applied to patients only when necessary. In our study, elective coronary angiography was applied to eligible patients with suspected stable obstructive CAD (Toshiba Infinix-i, Japan). We excluded patients who had a history of an ongoing acute coronary syndrome (ACS), a coronary artery bypass graft operation, a valvular surgery, or who had a heart transplant. Obstructive CAD was defined as 50% or more stenosis in the left main coronary artery and 70% or more stenosis in a large epicardial vessel or its

branches according to the recommendations of AHA/ACC (7-9).

Statistical Analysis

Descriptive statistics were presented as frequency (percentage) for categorical variables and mean±SD for the age of patients. The difference between the methods was analyzed by the McNemar test for variables with two categories, and the McNemar-Bowker test for variables with multiple categories. The agreement between the methods was analyzed by Kappa statistics or Kendall's Tau b statistics according to the number of categories. Univariate and multivariate logistic regression models were established for MPS status and angiographic status / classes. A p-value of less than 0.05 was considered a statistically significant result. The analyses were performed by SPSS 20.0 (IBM Inc, Chicago, USA).

Power Analysis

The power analysis of the study was performed by GPower 9.1.2 software (Universiaet Kiel, Germany). The sample size was calculated as 98 for the McNemar Exact test with one tail. The error was considered as 5%, the power as 0.90, and the proportion of the discordant pair as 0.80.

Results

A total of 104 patients who underwent angiography were included in the study. Male and female ratios were close to each other and calculated as 1.0:1.1. The average age of the patients was found to be 61.61±10.12 (26 - 81) years. Approximately half of the patients (47.1%) were diagnosed with hypertension and 30.8% with diabetes. While the rate of patients with hyperlipidemia was 33.7%, 11.5% of the patients had obesity. The smoking rate was 19.2% and the majority of female patients (87%) were in menopause.

There was no significant difference between the two methods in the evaluation of general MPS and angiography positivity (p=0.263). The agreement value of the results of the two methods was found to be significant (Kappa=0.602; p<0.001). The accuracy in detecting positivity between the two methods was calculated as 80.8%. While the results of measurements performed by the two methods in the LAD evaluation with MPS and angiography were found to be quite similar (p=0.791), the agreement value was found to be significant (Kappa=0.694; p <0.001, Accuracy: 86.5%). CX measurement results with MPS and angiography were also found to have quite high agreement and accuracy values (Kappa=0.462; p<0.001;

Accuracy: 85%). The difference between the measurements made by the two methods was not significant ($p=0.302$). There was no significant difference between the RCA evaluation results obtained with MPS and angiography ($p=0.227$). The accuracy between the two measurements was 89.4%, while the agreement value was also quite high (Kappa=0.667; $p<0.001$).

When the SSS and the angiography groups were compared, it was seen that the two measurement evaluations were significantly different from each other ($p=0.001$). SSS classification was evaluated in three groups as groups 1, 2, and 3. The angio classes were organized into <50%, 50-70% and >70% groups. The agreement value between the two measurements was moderate but statistically significant

Table 1 Comparison of patient characteristics and methods

		Angiography			p	Agreement p
		Negative	Positive			
Age	mean±SD	58,58±10,48	66,66±7,13	<0,001		
Gender N(%)	Woman	38 (64,4)	17 (37,8)	0,007		
	Man	21 (35,6)	28 (62,2)			
		Angiography			McNemar-Bowker p	Agreement p
		Negative	Positive			
MPS Evaluation	Negative	52 (88,1)	13 (28,9)	0,263	Kappa=0,602 <0,001	
	Positive	7 (11,9)	32 (71,1)			
MPS LAD	Negative	63 (91,3)	8 (22,9)	0,791	Kappa=0,694 <0,001	
	Positive	6 (8,7)	27 (77,1)			
MPS Cx	Negative	80 (94,1)	10 (52,6)	0,302	Kappa=0,462 <0,001	
	Positive	5 (5,9)	9 (47,4)			
MPS RCA	Negative	78 (96,3)	8 (34,8)	0,227	Kappa=0,667 <0,001	
	Positive	3 (3,7)	15 (65,2)			
SDS	>%10	7 (100)	25 (78,1)	0,001	0,091 0,172	
	<%10	0	7 (21,9)			
		<%50	%50-%70	>%70		
SSS	1.group (4-8)	57 (98,3)	1 (50)	31 (72,1)	0,001	Kendall's tau-b=0,373 0,014
	2. Group (9-12)	1 (1,7)	0	4 (9,3)		
	3.group (>13)	0	1 (50)	8 (18,6)		
SDS	>%10	7 (100)	1 (100)	24 (77,4)		Kendall's tau-b=0,234 0,014
	<%10	0	0	7 (22,6)		

MPS: Myocardial Perfusion Scintigraphy, LAD: Left Anterior Descending, Cx: Circumflex, RCA: Right Coronary Artery, SSS: Sum stress score, SDS: Sum difference score

(Kendall's tau-b=0.373; p=0.014).

A comparison was made between the SDS groups and angiography positivity evaluations. The two evaluation results were found to be significantly different (p<0.001). Moreover, the agreement value was not found to be significant as a result of the two evaluations (Kappa=0.091; p=0.172). Since there were two SDS groups and three angiography groups, no significant comparison was made between the two measurements, but the agreement value was found to be significant at a low level (Kendall's tau-b=0.234; p=0.014). The results are presented in detail in Table 1.

In the univariate logistic regression analysis performed according to the MPS positivity evaluation, the effect of prognostic factors was attempted to be determined. Age, gender, menopause, DM, HT, HL,

obesity and smoking statuses were included in the model as independent variables. Among the factors, only the age variable was observed to significantly increase the MPS positivity (OR=1.113 (1.051-1.177); p<0.001). Being male (OR=6,250 (2,081-18,513)), HL (OR=7,042 (2,291-21,736)) and an advanced age (OR=1,133 (1,062-1,208)) were found to be significant factors in the model established for evaluation of angiography positivity (p=0.001).

In the multivariate logistic regression model established by determining the 1st group among the SSS classes as the reference category, it was found that only smoking significantly affected both the 2nd group (p=0.013) and the 3rd group (p=0.044). In the model established by setting the <50% class as a reference for angiography classes, a significant effect of the male gender (p=0.001) and HL (p=0.001) were observed only in the >70% class (Table 2).

Table 2 Factors affecting the evaluation results of patients

MPS Positive				
	Beta	p	OR	95% CI
Age	0,107	<0,001	1,113	1,051-1,177
Gender (M)	0,485	0,486		
DM	0,355	0,551		
HT	0,740	0,390		
HL	0,941	0,332		
Obesity	0,138	0,710		
Smoking	2,663	0,103		
Menopause	0,054	0,817		
Angiography Positive				
Gender(M)	1,830	0,001	6,250	2,081-18,513
Age	0,124	<0,001	1,133	1,062-1,208
HL	1,951	0,001	7,042	2,291-21,736
SSS				
2. Group (9-12)				
Smoking	2,681	0,013	14,705	1,751-43,562
SSS				
3. Group (>13)				
Smoking	1,799	0,044	6,061	1,048-34,482
Angiography				
3. Group (>%70)				
Gender (M)	1,791	0,001	5,988	1,992-18,182
HL	1,839	0,001	6,28	2,024-19,607

MPS: Myocardial Perfusion Scintigraphy, SSS: Sum stress score, DM: Diabetes mellitus, HL: Hyperlipidemia, HT: Hypertension

Discussion

F.A. Enein et al. in their study comparing MPS and coronary angiography in 228 patients, found no significant difference between the two methods in evaluating MPS and angiography positivity. Similarly, to our study (80.8%), they calculated the accuracy rate in detecting positivity between the two methods as 80.49% (10). Shelley et al., in their study where they compared MPS and coronary angiography in 99 patients, obtained 87% sensitivity and 80% specificity in MPS (11). Fard-Esfehani et al., in their study comparing MPS and coronary angiography, revealed 91.2% sensitivity and 86.6% specificity in MPS (12). Fiechter et al., in their study comparing MPS and coronary angiography, obtained 87% sensitivity and 67% specificity in MPS (13). These studies also emphasize the importance of the diagnostic value of MPS, similar to our study.

William D. et al., in their study investigating the prognostic value of quantitative data in MPS, found an increased risk gradient for CAD with an increase in SSS (3). In our study, we observed an increase in coronary angiography positivity with an increase in SSS. The agreement value between the SSS classes (<8, 9-13, >13) and coronary angiography classes (<50%, 50-70%, >70%) was found to be moderately significant.

SDS is used to describe the extent of reversibility of ischemia. Numerous studies have shown that patients with an SDS over 10% benefit from revascularization (6). Berman et al., in their study investigating the prognostic value of quantitative data in MPS, found that the degree of reversible ischemia decreases as SDS decreases (14). Supporting this finding, our study showed that all patients with SDS<10 were patients with over 70% stenosis in coronary angiography.

Conclusion

In our study, the general quantitative evaluation of MPS, independent of visual evaluation, was found to have a high predictive value for CAD. A high accuracy rate was found in detecting positivity between the perfusion defected myocardial walls and the related left ventricular coronary vessels. However, the rates of detailed myocardial perfusion scoring (SSS and SDS) to detect CAD were not at a sufficient level. Therefore, we suggest that detailed myocardial perfusion scoring alone will be insufficient in detecting CAD, and should not be used alone. Studies to be conducted with a higher number of patients are needed regarding the predictive and prognostic value of myocardial perfusion scoring.

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