Effect of Localization of Coronary Artery Lesions on Total Perfusion Deficit in Myocardial Perfusion Scintigraphy

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ABSTRACT

Introduction: In the present study, we analyzed patients with stable coronary artery disease (SCAD) by quantitative myocardial perfusion scintigraphy and evaluated the effect of different coronary lesion locations on total perfusion deficit (TPD).

Patients and Methods: A total of 133 consecutive patients with SCAD who underwent myocardial perfusion imaging single photon emission computed tomography (SPECT) and conventional coronary angiography according to SPECT results were included in the study. TPD was used as the automated quantification variable.

Results: Of the patients, 61 had significant coronary artery disease, and 72 had normal coronary arteries. For the normal, left anterior descending artery (LAD), circumflex artery (CX), and right coronary artery (RCA) groups, the median values were 7% vs. 11% vs. 10% vs. 9%, 4% vs. 6% vs. 7% vs. 4%, and 3% vs. 5% vs. 6% vs. 3% for stress TPD (sTPD), rest TPD (rTPD), and ischemic TPD (iTPD), respectively. There was no statistically significant difference in quantitative analysis (sTPD, rTPD, and iTPD) between the LAD, CX, and RCA groups ($p > 0.05$).

Conclusion: TPD obtained by quantitative analysis method can be used for all coronary artery lesion location.

Key Words: Stable coronary artery disease; total perfusion deficit; SPECT

Miyokart Perfüzyon Sintigrafisinde Koroner Arter Lezyonlarının Lokalizasyonunun Total Perfüzyon Defekti Üzerine Etkisi

ÖZET

Giriş: Bu çalışmada kantitatif miyokart perfüzyon sintigrafisi ile stabil koroner arter hastalığı olan hastaları inceledik ve farklı koroner lezyon lokasyonlarının total perfüzyon defekti üzerine olan etkisini değerlendirdik.

Hastalar ve Yöntem: Stabil koroner arter hastalığı olan miyokardiyal perfüzyon görüntüleme-SPECT yapılan ve SPECT sonuçlarına göre konvansiyonel koroner anjiyografiye alınmış 133 ardışık hasta çalışmaya alındı. Kantitatif inceleme değişkeni olarak total perfüzyon defekti (TPD) kullanıldı.

Bulgular: Atmış bir hastada anlamlı koroner arter hastalığı ve 72 hastada normal koroner arter vardı. Normal, LAD, CX ve RCA grupları için medyan değerler sTPD (sırasıyla %7, %11, %10, %10), rTPD (sırasıyla %4, %6, %7, %4,) ve iTPD (sırasıyla %3, %5, %6, %3) idi. Kantitatif analizde (sTPD, rTPD ve iTPD) LAD, CX ve RCA grupları arasında istatistiksel olarak anlamlı fark yoktu ($p > 0.05$).

Sonuç: Kantitatif analiz yöntemiyle elde edilen total perfüzyon defisiti tüm koroner arter hastalığı lokalizasyonları için kullanılabilir.

Anahtar Kelimeler: Kararlı koroner arter hastalığı; total perfüzyon defisiti; SPECT

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INTRODUCTION

Stable coronary artery disease (SCAD) emerges with reversible ischemia–hypoxia attacks generally due to physical and emotional stress. SCAD is commonly caused by atheromatous plaque that obstructs or gradually narrows the epicardial coronary arteries. Non-invasive stress tests that are performed taking into account the Bayesian principles reveal further guidance for not only diagnosis but also therapeutic approaches. Both quantitative and semi-quantitative analyses of myocardial perfusion scintigraphy (MPS) are widely used in this field.

There are studies validating the semi-quantitative analysis by using MPS for the diagnosis of SCAD or risk assessment of patients with known SCAD[1]. On the other hand, a close linear correlation between total perfusion deficit (TPD), which is an automated quantitative myocardial perfusion imaging using single-photon emission computed tomography (MPI-SPECT), value based on normal data files and expert visual analysis had been reported previously[1,2].

Technological progress in computer hardware and software tends to shorten the acquisition time and allows reduction of the dose of the administered radiopharmaceutical and radiation burden to patients[1-3].

The aim of the present study was to investigate both the utilization of automated quantification for detecting different coronary artery lesions and the effect of lesion location to quantitative analysis values in patients with SCAD.

PATIENTS and METHODS

This was a retrospective study. The total referral population for MPS scan from March 2016 to February 2017 included 1321 patients. Patients with a history of previous percutaneous intervention, coronary artery bypass grafting, and who underwent coronary angiography at another center were excluded from the study. A total of 133 consecutive patients with suspected SCAD who underwent ^{99m}Tc-sestamibi stress/rest MPI-SPECT and conventional coronary angiography according to SPECT results were included in the study.

Image Acquisition and Reconstruction Protocol

Studies were performed using ^{99m}Tc-sestamibi stress and ^{99m}Tc-sestamibi rest two-day protocol. Patients fasted > 6 h before the study. Patients underwent exercise treadmill testing for stress study, and they were injected intravenous 10 to 12 mCi (370 to 444 MBq) ^{99m}Tc-sestamibi at peak exercise and then continued the exercise for 1 min. The following day, rest study was performed with the same dose administered for the stress study. SPECT images were acquired 15 to 60 min after tracer injection using the IQ-SPECT Symbia S system (Siemens, USA) gamma camera system with dedicated multifocal SMARTZOOM™ collimators performing cardiocentric acquisition. SPECT tomograms were reconstructed and reoriented by using an automatic algorithm system as described in previous studies[1,2]. Images were processed using Cedars-Sinai quantitative perfusion SPECT (QPS) software.

A five-point scale (0, normal; 1, mildly decreased; 2, moderately decreased; 3, severely decreased; and 4, absence of segmental uptake) and 17-segment model was used to obtain summed stress scores (SSSs), summed rest scores (SRSs), and summed difference scores (SDSs) for semi-quantitative visual analysis. Images were scored by consensus opinion by two expert readers. SSS and SRS were calculated by summing the 17-segment stress and rest scores, respectively. SDS was obtained by subtracting SRS from SSS.

Automated Quantification of MPI-SPECT

We used TPD as the automated quantification variable. The TPD measurement was computed automatically as the integral of polar map severities below the abnormality threshold, reflecting both extent and severity of the defect. TPD scores were measured at stress and rest images using the QPS software. We calculated the ischemic TPD (iTPD) from the difference between stress TPD (sTPD) and rest TPD (rTPD).

Coronary Angiography

Coronary angiography was performed via the femoral percutaneous approach using a Siemens Angiocore (Germany) by experienced interventional cardiologists, performing at least 75 interventional procedures annually.

Statistical Analysis

Statistical analyses were performed using the SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation. Categorical variables were expressed as percentages (%). Continuous variables were analyzed using the Kolmogorov–Smirnov test for normal distribution. Comparisons between the normally distributed data were performed by the Student's t-test. The Mann-Whitney U test was used for data that were not normally distributed. The chi-square test was applied to compare the influence of categorical variables. A p value of < 0.05 was considered as significant. Receiver operating characteristic curves were generated to compare quantitative and semi-quantitative parameters versus conventional angiography results. The cut-off values for sTPD and iTPD were determined from the intersection of the sensitivity and specificity curves graphed by the quantification value in the entire cohort of patients to maximize both sensitivity and specificity. Sensitivity, specificity, positive and negative predictive values, and accuracy for the prediction of obstructive coronary artery disease (CAD) were obtained from these curves. The areas under the curve (AUCs) were compared using the Delong Clarke-Pearson method.

RESULTS

Of the patients, 21 (8.5%) had significant left anterior descending artery (LAD) lesion, 21 (8.5%) had significant circumflex artery (Cx) lesion, 19 (7.7%) had significant right coronary artery (RCA) lesion, and 72 (29.3%) had normal coronary artery. Table 1 shows the patient characteristics as illustrated according to their coronary angiography findings. There were no significant differences in terms of basic laboratory findings and risk factors between the four groups.

SSS, SRS, SDS, stress (s) TPD, rest (r) TPD, and ischemic (i) TPD were estimated for each of the 133 patients, and their mean values and minimum and maximum ranges were calculated for each patient. Table 2 shows the median, mean, and minimum–maximum values acquired from this analysis.

For the normal, LAD, CX, and RCA groups, the median values were 4 vs. 8 vs. 8 vs. 6, 3 vs. 2 vs. 3 vs. 4, 1 vs. 4 vs. 4 vs. 3, 7% vs. 11% vs. 10% vs. 9%, 4% vs. 6% vs. 7% vs. 4%, and 3% vs. 5% vs. 6% vs. 3% for SSS, SRS, SDS, sTPD, rTPD, and iTPD, respectively (Table 2). As expected, both quantitative and semi-quantitative values were higher in the LAD, CX, and RCA groups than in the normal group ($p< 0.05$ for all). There was no statistically significant difference in quantitative analysis (sTPD, rTPD, and iTPD) between the LAD, CX, and RCA groups ($p> 0.05$).

The AUC analysis was also performed to evaluate the ability of the quantification to predict significant stenosis of coronary arteries. Cut-off point, sensitivity, specificity, and p value were calculated for sTPD, rTPD, and iTPD. For detecting ischemia, the optimal cut-off points were 8.5 (Se 65% and Sp 59%), 4.5 (Se 53% and Sp 53%), and 3.5 (Se 50% and Sp 57%) for sTPD, rTPD, and iTPD, respectively (Table 3).

DISCUSSION

Our study revealed higher sTPD, rTPD, and iTPD values in the patient groups with significant coronary artery lesions than in the normal coronary artery group. As expected, semi-quantitative values were also significantly higher in these groups. These results showed that the utilization of TPD is useful to determine the underlying SCAD in patients with stable angina pectoris.

While the prevalence of SCAD has increased because of the improvements in diagnostic tools, mortality has decreased, and prognosis in this population is getting better. MPS, a valuable prognostic test in CAD, is widely used to determine the need for catheterization[4-7]. Semi-quantitative analysis, which has highly operator-dependent accuracy, is widely used in MPS. TPD, a very useful novel quantitative analysis modality, reduces the operator dependency[8].

Physicians commonly face the choice of recommending revascularization versus medical therapy in patients with SCAD. Based on multiple, prospective randomized clinical trials comparing these alternatives, extensive evidence exists to support the selection of one therapy versus the other in a variety of clinical and angiographic patient subsets. However, only limited, unadjusted studies compare survival with revascularization versus medical therapy after MPS. Revascularization provides more survival benefit over medical therapy with increasing amounts of inducible ischemia. Higher amount of inducible ischemia in LAD, CX, and RCA patients supports the revascularization decision.

Table 1. Basic characteristics, risk factors, and laboratory findings of the patients

	Normal	LAD	CX	RCA	p
Age (years)	60.9 ± 9.8	61.7 ± 13.4	60.1 ± 8.5	57.9 ± 11.4	> 0.05
Sex (% male)	94	83	82	94	> 0.05
Diabetes mellitus (%)	21	17	19	26	> 0.05
Hypertension (%)	50	45	53	43	> 0.05
Smoking (%)	52	42	64	42	> 0.05
Family history of CAD (%)	23	33	24	22	> 0.05
Glucose (mg/dL)	138.9 ± 59.6	136.2 ± 55.3	152.0 ± 64.5	152.0 ± 91.6	> 0.05
Urea (mg/dL)	36.6 ± 13.4	32.6 ± 16.6	33.7 ± 8.5	35.8 ± 7.8	> 0.05
Creatinine (mg/dL)	0.9 ± 0.3	0.8 ± 0.2	0.8 ± 0.1	0.8 ± 0.1	> 0.05
Total cholesterol (mg/dL)	224.9 ± 59.6	236.7 ± 71.2	228.0 ± 53.5	223.0 ± 31.4	> 0.05
Low-density lipoprotein (mg/dL)	145.7 ± 48.2	159.0 ± 56.9	148.2 ± 45.7	142.6 ± 34.2	> 0.05
High-density lipoprotein (mg/dL)	44.6 ± 10.3	44.6 ± 10.1	41.9 ± 9.8	44.3 ± 7.7	> 0.05
Triglyceride (mg/dL)	177.2 ± 101.9	183.2 ± 110.7	196.9 ± 115.3	148.6 ± 52.1	> 0.05
White blood cell count ($10^3/\mu L$)	4.5 ± 4.2	5.0 ± 4.2	4.8 ± 4.3	4.7 ± 4.1	> 0.05
Hemoglobin (g/dL)	13.5 ± 1.4	13.8 ± 1.3	14.7 ± 1.8	13.4 ± 1.4	> 0.05

CX: Circumflex artery, LAD: Left anterior descending artery, Normal: Normal coronary arteries, RCA: Right coronary artery, CAD: Coronary artery disease.

Table 2. The comparison of the quantitative and semi-quantitative values of the patients

		Mean ± standard deviation	Median	Min-Max	p
SSS	Normal	5.2 ± 4.1	4	0-33	< 0.05 normal-LAD, CX, RCA
	LAD	9.0 ± 6.9	8	2-24	
	CX	8.2 ± 7.2	8	0-19	> 0.05 LAD-CX, LAD-RCA, RCA-CX
	RCA	6.0 ± 4.7	6	2-15	
SRS	Normal	3.3 ± 4.9	3	0-27	< 0.05 normal-LAD, CX, RCA
	LAD	4.6 ± 5.5	2	0-17	
	CX	3.5 ± 3.9	3	0-10	> 0.05 LAD-CX, LAD-RCA, RCA-CX
	RCA	3.7 ± 2.8	4	0-9	
SDS	Normal	2.1 ± 2.4	1	0-12	< 0.05 normal-LAD, CX, RCA
	LAD	4.2 ± 2.1	4	1-8	
	CX	4.1 ± 3.0	4	0-8	> 0.05 LAD-CX, LAD-RCA, RCA-CX
	RCA	2.2 ± 2.4	3	0-6	
sTPD (%)	Normal	8.8 ± 8.2	7	0-45	< 0.05 normal-LAD, CX, RCA
	LAD	13.7 ± 10.7	11	1-34	
	CX	11.8 ± 10.0	10	0-25	> 0.05 LAD-CX, LAD-RCA, RCA-CX
	RCA	8.5 ± 6.6	9	1-20	
rTPD (%)	Normal	5.5 ± 7.2	4	0-41	< 0.05 normal-LAD, CX, RCA
	LAD	9.1 ± 9.7	6	0-27	
	CX	7.2 ± 6.9	7	0-18	> 0.05 LAD-CX, LAD-RCA, RCA-CX
	RCA	4.0 ± 4.0	4	0-13	
iTPD (%)	Normal	3.5 ± 2.5	3	0-11	< 0.05 normal-LAD, CX, RCA
	LAD	4.5 ± 3.2	5	1-10	
	CX	4.5 ± 3.5	6	0-9	> 0.05 LAD-CX, LAD-RCA, RCA-CX
	RCA	4.5 ± 3.8	3	0-11	

CX: Circumflex artery, LAD: Left anterior descending artery, RCA: Right coronary artery, SSS: Summed stress score, SRS: Summed rest score, SDS: Summed difference score, TPD: Total perfusion deficit, sTPD: Stress TPD, rTPD: Rest TPD, iTPD: Ischemic TPD.

Table 3. Cut-off points for detecting significant coronary artery disease

	Cut-off point	AUC	Se (%)	Sp (%)	p
sTPD (%)	8.5	0.578	65	59	< 0.05
rTPD (%)	4.5	0.537	53	57	< 0.05
iTPD (%)	3.5	0.567	50	57	< 0.05

AUC: Area under curve, Se: Sensitivity, Sp: Specificity, TPD: Total perfusion deficit, sTPD: Stress TPD, rTPD: Rest TPD, iTPD: Ischemic TPD.

Patients with stress-induced reversible perfusion deficits 10% of the total LV myocardium (≥ 2 of the 17 segments) represent a high-risk subset[9-12]. Early coronary arteriography should be considered in these patients. In these patients with 10% ischemic myocardium, revascularization was associated with a 50% risk-adjusted reduction in cardiac death. A 10% admitted border is a semi-quantitative value because it is acquired by transformation of SDS value to % myocardium. It is possible to perform less operator-dependent measurements using TPD values.

In previous studies, the reliability of TPD was commonly evaluated; however, there was no comparative assessment of TPD values for different coronary artery lesion localization. In our study, TPD values for LAD, CX, and RCA lesions are evaluated separately. As a result, there was no statistically significant difference in sTPD, rTPD, and iTPD values obtained from quantitative analysis of MPS between coronary artery lesions in various locations (LAD, CX, and RCA). This result shows that the usage of TPD for diagnostic purpose in all CAD

locations is feasible. Cut-off values of 8.5% for sTPD, 4.5% for rTPD, and 3.5% for iTPD (Se 65%-50% and Sp 59%-57%) were defined with quantitative analysis for detecting significant CAD (angiographically > 70% narrowing) according to this evidence. These values will aid us in terms of revascularization decision.

Automated quantitative analysis systems are incorporated into most SPECT camera computer equipment. Some of the most common are Emory Toolbox, Cedars QPS, and 4D-MSPECT[13-15]. We can estimate subtle changes in ischemic burden during follow-up of the same patient. In addition, this image change analysis can provide an objective measurement of a patient's response to therapy. This small but clinically important improvement can be under interpreted because of the subjective scoring of different nuclear medicine specialists[16]. The diagnostic performance of these software packages was discussed in several studies[1,17].

In the recent guidelines, "quantitative analysis" is defined not only as a valuable supplement to the visual interpretation of perfusion data, but several studies have also documented better reproducibility and less interobserver variations[2,18-21]. There are also studies suggesting that the automated quantitative assessment with the local normal database is useful for the detection of CAD when experts in visual interpretation of a myocardial perfusion SPECT image were absent in a clinical setting[22].

In practice, the use of contemporary quantitative programs can improve image acquisition quality, as well as interpretation. Several dedicated hardware camera systems with optimized acquisition geometry, collimator design, and associated reconstruction software have been recently introduced by various vendors (Cardius XPO (Digirad, Inc., Poway, CA, USA), CardiArc (CardiArc, Canton, MI, USA), D-SPECT (Spectrum-Dynamics, Haifa, Israel), Discovery (GE, Milwaukee, WI, USA), IQ-SPECT (Siemens)[23]. The newer methods can further refine longitudinal follow-up by analyzing serial stress/rest studies together in pairs, thereby eliminating errors associated with multiple comparisons to normal limits and variations in contour placements[24,25]. Another advantage of this analysis is that it does not require normal limits[16].

There are studies recording the significant correlations between semi-quantitative and automated quantitative variables using the IQ-SPECT system similar to our study results[26]. In a new study, automated analysis showed higher sensitivity but lower specificity. This means that slightly higher sensitivity of automated analysis in trade off a lower specificity could be more preferable because missing obstructive CAD due to a false-negative SPECT might outweigh the number of 'unnecessary' invasive angiograms. They concluded that automated analysis of myocardial perfusion SPECT can be as accurate as visual interpretation detecting significant CAD as defined by fractional flow reserve[27].

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: CD, FÇ, NÖ, CK
Analysis/Interpretation: CD, FÇ, ZB, AK, MÇ, BG
Data Acquisition: CD, AK, MÇ, BG
Writting: CD, FÇ, NÖ, CK
Critical Revision: CD, NÖ, ZB, CK, AU, RA, TU, AH, ÖA
Final Approval: All of authors

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