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

Running Head: Validity of Total Perfusion Deficit in all coronary lesion locations.

Cem Doğan1, Zübeyde Bayram1, Ferahnaz Çınaral2, Abdülkadir Uslu1, Rezzan Deniz Acar1, Çağatay Önal1, Murat Çap1, Büşra Güvendi1, Tuba Unkun1, Ahmet Karaduman1, Aykun Hakgör1, Özgür Yaşar Akbal1, Cihangir Kaymaz1, Nihal Özdemir1

1 İstanbul Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, İstanbul, Türkiye

2 İstanbul Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Nükleer Tıp Kliniği, İstanbul, Türkiye

Abstract

Background: In this study, we analyzed patients with stable coronary artery disease by quantitative myocardial perfusion scintigraphy and evaluated the effect of different coronary lesion locations on total perfusion deficit.

Material and Method: Study included 133 consecutive patients with stable coronary artery disease who underwent myocardial perfusion imaging-SPECT and conventional coronary angiography according to SPECT results. Total perfusion deficit (TPD) was used as the automated quantification variable.

Results: Sixtyone patients had significant coronary artery disease and 72 patients had normal coronary arteries. For Normal, LAD, CX and RCA groups, the median values of sTPD were (%7 vs %11 vs %10 vs %9), rTPD were (% 4 vs %6 vs %7 vs %4) and iTPD were (%3 vs %5 vs %6 vs %3) respectively. There were no statistically significant difference in quantitative analysis (sTPD, rTPD and iTPD) between the LAD, CX and RCA groups ($p>0.05$).

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

Key Words: Stable Coronary Artery Disease, Total Perfusion Deficit, SPECT

 DOI: 10.5578/khj.67215

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

Kısa Başlık : Total perfüzyon defektinin tüm koroner lezyon yerleşimlerinde geçerliliği.

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

Gereç 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 (sırasyla % 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 Sözcükler: Kararlı koroner arter hastalığı, total perfüzyon defisiti, SPECT

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 stres tests which are performed with taking into account the Bayesian principles reveals further guidance for not only diagnosis but also therapeutic approaches. Both quantitative and semi-quantitative analysis of myocardial perfusion scintigraphy (MPS) is widely used in this field.

There are studies validating the semi-quantitative analysis by using MPS for the diagnosis of SCAD or risk assesement 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 upon normal data files and expert visual analysis had been reported previously (1,2).

Technological progress in computers' hardware and software tends to shorten the acquisition time, and allows reduction of the dose of the administrated radiopharmaceutical (rph) and radiation burden to patients (1-3).

The aim of this study is both investigating 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.

Material and Methods:

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

Image Acquisition and Reconstruction Protocole:

Studies were performed using ^{99m}Tc-sestamibi stress and ^{99m}Tc-sestamibi rest two day protocole. Patients fasted >6 hours (h) before the study. Patients underwent exercise treadmill testing for the stress study and they were injected i.v. 10 to12mCi (370 to 444MBq) ^{99m}Tc-sestamibi at peak exercise and than 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 minutes after tracer injection using IQ-SPECT Symbia S system (Siemens, USA) gamma camera system with dedicated multifocal SMARTZOOM™ collimators

 DOI: 10.5578/khj.67215

performing cardiocentric acquisition. SPECT tomograms were reconstructed and reoriented by using an automatic algorithm system described in previous studies (1,2). Images were processed using Cedars-Sinai quantitative perfusion SPECT (QPS) software.

Five point scale (0, normal; 1, mildly decreased; 2, moderately decreased; 3, severely decreased; and 4, absence of segmental uptake) and seventeen segment model was used to obtain summed stress scores (SSS), summed rest scores (SRS) and summed difference scores (SDS) for semiquantitative 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. The SDS was obtained by subtracting SRS from SSS.

Automated Quantification of SPECT MPI:

We used TPD as the automated quantification variable. The TPD measure 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 QPS software. We calculated the ischemic TPD from difference between stress TPD and rest TPD.

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 SPSS software version 20.0. Continuous variables were presented as mean±standard deviation (SD) and categorical variables were expressed as percentages. Continuous variables were analyzed with Kolmogorov–Smirnov to test normal distribution. Comparisons between the normally distributed data were performed by Student’s t-test. Mann Whitney U test was used for the data that were not normally distributed. Chi-square test was applied to compare the influence of categorical variables. A p value of <0.05 was considered as significant. Receiver operating curves were generated to compare quantitative and semiquantitative parameters versus conventional angiography results. Cut-off values for sTPD, 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 were obtained from these curves. Areas under the curve were compared using the Delong Clarke-Pearson method.

 DOI: 10.5578/khj.67215

Results:

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

SSS, SRS, SDS, stres (s) TPD, rest (r) TPD and ischemic (i) TPD were estimated for each 133 patients and their mean values, minimum and maxiumum ranges were calculated for each patient. Median, mean and minimum-maximum values acquired from this analysis are shown in Table-2.

For Normal, LAD, CX and RCA groups the median values of SSS were (4 vs 8 vs 8 vs 6), SRS were (3 vs 2 vs 3 vs 4), SDS were (1 vs 4 vs 4 vs 3), sTPD were (%7 vs %11 vs %10 vs %9), rTPD were (% 4 vs %6 vs %7 vs %4) and iTPD were (%3 vs %5 vs %6 vs %3) respectively (Table 2). As expected, both quantitative and semi-quantitative values revealed higher in LAD, CX and RCA groups than Normal group. ($p<0.05$ for all) There was no statistically significant diferrence 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, spesifity and a *p* value were calculated for sTPD, rTPD and iTPD. For detecting the ischemia the optimal cut off point for stressTPD was 8,5 (Se %65, Sp%59), for rTPD was 4,5(Se %53, Sp%53) and for iTPD was 3,5 (Se %50, Sp%57) (Table 3).

Discussion:

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

While prevelance of SCAD has increased beacuse of the improvements in diagnostic tools, mortality has decreased and prognosis in this population is getting better**.** MPS, a valuable prognostic test in coronary

 DOI: 10.5578/khj.67215

artery disease (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. On the basis of 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, RCA patients supports the revascularization decision.

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. These patients with 10% ischemic myocardium, revascularization was associated with a 50% risk-adjusted reduction in cardiac death. 10% admited 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 with using TPD values.

At previous studies, reliability of TDP was commonly evaluated however there was not comparative assessment of TDP values for different coronary artery lesion localization. In our study, TPD values for LAD, CX and RCA lesions are evaluated seperately. 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, RCA). This result shows us the usage of TPD for diagnostic purpose in all coronary artery disease locations is feasible. Cut off values of 8.5% for sTPD, 4.5% for rTPD, 3.5% for iTPD (Se 65-50%, Sp 59-57%) was defined with quantitative analysis for detecting significant coronary artery disease (angiographically >70% narrowing) according to this evidence. This values will help 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 also this image change analysis can provide an objective measure of a patient’s response to therapy. This small, but clinically important improvements can be under interpreted because of the subjective scoring of different nucleer medicine specialists. (16). Diagnostic performance of these software packages were discussed in several studies (1,17).

In the recent guidelines “Quantitative analysis” defined as not only a valuable supplement to the visual interpretation of perfusion data (18), but several studies have also documented better reproducibility and less interobserver variations (2,19-21). 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.]; CardiArc [CardiArc]; and D-SPECT [Spectrum-Dynamics]), Discovery (GE), 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). An other advantage of this analysis is that it does not require normal limits (16).

There are studies recording significant correlations between semi-quantitative and automatic-quantitative variables using IQ-SPECT system similar to our study results (26). In a new study automated analysis showed higher sensitivity, but lower specificity. This means 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 defined by FFR (27).

REFERENCES

1. Klocke FJ, Baird MG, Lorell BH, Bateman TM, Messer JV, Berman DS, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging-executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Cardiac Radionuclide Imaging). J Am Coll Cardiol 2003; 42: 1318 – 1333.
2. Berman DS, Kang X, Gransar H, Gerlach J, Friedman JD, Hayes SW, et al. Quantitative assessment of myocardial perfusion abnormality on SPECT myocardial perfusion imaging is more reproduciblethan expert visual analysis. J Nucl Cardiol 2009; 16: 45 – 53.
3. Keiichiro Yoshinaga, MD, PhD; Takayuki Matsuki, MD, PhD; Akiyoshi Hashimoto, MD, PhD; Kazumasa Tsukamoto, PhD; Tomoaki Nakata, MD, PhD; Nagara Tamaki, MD, PhD. Validation of Automated Quantitation of Myocardial Perfusion and Fatty Acid Metabolism Abnormalities on SPECT Images. Circ J. 2011;75(9):2187-95. Epub 2011 Jul 12.
4. Hachamovitch R, Berman DS, Kiat H, Bairey CN et al. Effective risk stratification using exercise myocardial perfusion SPECT in women gender-related differences in prognostic nuclear testing. J Am Coll Cardiol 1996, 28(1):33-44
5. Hachamovitch R, Berman DS, Kiat H, Bairey CN et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: incremental prognostic value and use in risk stratification. Circulation 1996, 93(5):905-914
6. Hachamovitch R, Rozanski A, Shaw LJ, Stone GW et al. İmpact of ischemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical theraphy among patients undergoing stres-rest myocardial perfusion scintigraphy. Eur Heart J 2011, 32(8): 1012-1024
7. Iskander S, Iskandrian AE: Risk assesment using single-photon emission computed tomographic technetium-99m sestamibi imaging. J Am Coll Cardiol 1998, 32(1) 57-62
8. Slomka PJ, Nishina H, Berman DS et al. Automated quantification of myocardia perfusion SPECT using simplified normal limits. J Nucl Cardiol 2005:12:66-77.

9. Lin FY, Dunning AM, Narula J et al. Impact of an Automated Multimodality Point-of-Order Decision Support Tool on Rates of AppropriateTesting and Clinical Decision Making for Individuals With Suspected Coronary Artery Disease: A Prospective Multicenter Study. J Am Coll Cardiol. 2013;62(4):308–16

10. Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging. A diagnostic tool comes of age. Circulation 1991;83:363–381.

11. Hachamovitch R, Berman DS, Shaw LJ, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. Circulation 1998;97:535–543.

12. Hachamovitch R, HayesSW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation 2003;107:2900–2907.

13. Germano G, Kavanagh PB, Slomka PJ, Van Kriekinge SD, Pollard G, Berman DS. Quantitation in gated perfusion SPECT imaging: The Cedars-Sinai approach. J Nucl Cardiol. 2007;14:433–54.

14. Ficaro EP, Lee BC, Kritzman JN, Corbett JR. Corridor4DM: the Michigan method for quantitative nuclear cardiology. J Nucl Cardiol. 2007;14:455–65.

15. Garcia EV, Faber TL, Cooke CD, Folks RD, Chen J, Santana C. The increasing role of quantification in clinical nuclear cardiology: the Emory approach. J Nucl Cardiol. 2007;14:420–32.

16. Slomka P, Hung GU, Germano G, Berman DS. Novel SPECT Technologies and Approaches in Cardiac Imaging. Cardiovasc Innov Appl. 2016 Dec 1;2(1):31-46

17. Sahiner I, Akdemir UO, Kocaman SA, Sahinarslan A, Timurkaynak T, Unlu M. Quantitative evaluation improves specificity of myocardial perfusion SPECT in the assessment of functionally significant intermediate coronary artery stenoses: a comparative study with fractional flowreserve measurements.Ann Nucl Med. 2013 Feb;27(2):132-9.

18. Holly TA, Abbott BG, Al-Mallah M, Calnon DA, Cohen MC, DiFilippo FP, et al. Single photon-emission computed tomography. J Nucl Cardiol. 2010;17:941–73.

19. Imbert L, Poussier S, Franken PR et al. Compared performance of high-sensitivity cameras dedicated to myocardial perfusion SPECT: a comprehensive analysis of phantom and human images. J Nucl Med2012; 53(12): 1897-903.

20. Verberne HJ, Acampa W, Anagnostopoulos C. EANM procedural guidelines for radionuclide myocardial perfusion imaging with SPECT and SPECT/CT: 2015 revision. Eur J Nucl Med Mol Imaging. 2015 Nov;42(12):1929-40.

21. Xu Y, Hayes S, Ali I, et al. Automatic and visual reproducibility of perfusion and function measures for myocardial perfusion SPECT. Journal of Nuclear Cardiology. 2010; 17(6):1050–7.

22. Arsanjani R, Xu Y, Hayes SW. Comparison of Fully Automated Computer Analysis and Visual Scoring for Detection of Coronary Artery Disease from Myocardial Perfusion SPECT in a Large Population. J Nucl Med. 2013 Feb;54(2):221-8.

23. Nakazato R, Tamarappoo BK, Kang X. Quantitative Upright–Supine High-Speed SPECT Myocardial Perfusion Imaging for Detection of Coronary Artery Disease: Correlation with Invasive Coronary Angiography.J Nucl Med. 2010 Nov;51(11):1724-31.

24. Slomka PJ, Nishina H, Berman DS, et al. Automatic quantification of myocardial perfusion stress-rest change: a new measure of ischemia. J Nucl Med. 2004; 45(2):183–91.

25. Prasad M, Slomka PJ, Fish M, et al. Improved quantification and normal limits for myocardial perfusion stress-rest change. J Nucl Med. 2010; 51(2):204–9.

26. Havel M, Kolacek M, Kaminek M. Myocardial perfusion imaging parameters: IQ- SPECTand conventional spect system comparison. Hell J Nucl Med. 2014 Sep-Dec;17(3):200-3.

27. Schumacher SP, Leipsic JA, Min JK, Knuuti J, Lammertsma AA, van Rossum AC, van Royen, et al. Automated SPECT analysis compared with expert visual scoring for the detection of FFR-definedcoronary artery disease. Eur J Nucl Med Mol Imaging. 2018 Jul;45(7):1091-1100