Prognostic value of myocardial perfusion imaging in Iranian patients using total perfusion deficits: Comparison with semi-quantitative assessment

Original Article

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ABSTRACT

Introduction: Considering that quantitative methods are usually more reproducible with lower inter-observer variability, the purpose of this research was to compare the prognostic value of the two quantitative method with quantitative perfusion SPECT (QPS) software.

Methods: This study was performed prospectively and included 200 participants who were referred for myocardial perfusion imaging. These participants were selected by the convenience sampling method. All patients were followed up after one year. Patients were classified as those with and without major cardiac events, including cardiac death, non-fatal myocardial infarction, open-heart surgery, abnormal angiographic findings, and unstable angina.

Results: There were 62 male (31.0%) and 138 female (69.0%) patients, ranging in age from 30 to 86 years. The results indicated that the major cardiac events were significantly higher in moderate and severe categories based on summed stress score (SSS) (P=0.024) and total perfusion deficit (TPDs) (P=0.002) scores. SSS score with TPDs score (P = 0.764), summed rest score (SRS) with TPDr score (P = 0.583) and SDS with ΔTPD (P = 0.118) were compatible for predicting major heart events within a year.

Conclusion: Total perfusion deficits obtained from QPS software is a useful method for predicting major cardiac events in patients with suspected cardiovascular disease (CVD). Predictive ability of TPD was similar to that of the semi-quantitative method with an expert interpreter's help. Moreover, this method can be helpful for CAD diagnosis and therapeutic evaluation of patients.

Key words: Myocardial perfusion imaging; Total perfusion deficits; Quantitative perfusion SPECT software

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INTRODUCTION

Despite progress in medical research, cardiovascular disease (CVD) is the third leading cause of death worldwide. Coronary artery disease (CAD) is the leading cause of death among CVD [1]. Population development and increasing the global population's average age result in rapid growing of this disease prevalence [2-4].

Nevertheless, diagnostic methods play an effective and accurate role in controlling and preventing CVD and its complications [5]. Among these diagnostic modalities, myocardial perfusion imaging (MPI) is a well-known non-invasive method for risk assessment in patients suspected of CAD.

The interpretation of MPI is mainly based on visual assessment. However, different semi-quantitative and quantitative analyses can help with more confident results. The semi-quantitative analysis relies on the segmental scoring system based on the physician's expertise. In contrast, the automated quantitative approach is based on the pixel relative values of perfusion. Total perfusion deficit (TPD) is a pixel-based objective parameter calculated automatically by quantitative perfusion SPECT (QPS) software. Quantitative automatic examination with TPD has been approved to show the extent and severity of defects correlated with the results of visual and semi-quantitative interpretations. However, these methods' role in the prognostic appraisal of suspected CAD patients requires more research [6].

Considering that quantitative methods are usually more reproducible with lower inter-observer variability, this may be a better option for quantitative assessment, particularly in serial studies [7, 8]. The purpose of this research was to compare the two quantitative method assessment's prognostic value with QPS software.

METHODS

This study was performed prospectively and has been approved by the Ethical Committee (IR.SUMS.REC.1394.S469) and Institutional Review Board of Shiraz University of Medical Sciences (No.7204) and informed consent form were signed by all of the patients included in the study.

Patient selection

This study included 200 participants who were referred to our center for myocardial perfusion imaging. These participants were selected by the convenience sampling method. The exclusion criteria were age of below 20, previous history of CAD, heart failure history, severe valvular disease or evidence of another structural heart disease, and patients with incomplete data or follow-up. Patients with low-quality scan results or the presence of any artifact interfering with quantitative results were also excluded.

MPI protocol

Myocardial perfusion imaging was performed according to the standard guidelines. According to the initial assessment, the stress phase was done as an exercise treadmill test with standard Bruce protocol or a pharmacologic test with dipyridamole or dobutamine.

In both stages of stress and rest, 15-20 mci [^{99m}Tc] Tc-MIBI was injected to patients, and imaging was performed about 15 minutes after stress with exercise and 45-60 minutes after drug stress and rest using a dual-head gamma camera. The SPECT acquisition was performed with 32 projections in a rotating arch of 180 degrees with a matrix size of 64*64. After the reconstruction of the SPECT images by filtered back-projection method, the left ventricular perfusion quantification was performed using QPS software and quantitative findings including TPD at both stress (TPDs) and rest phase (TPDr) and semi-quantitative parameters including summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS) were extracted. Based on the 20-segment model of the left ventricle, the semi-quantitative review was obtained by software and approved by a nuclear medicine expert, and updated or corrected if necessary. We also calculated the delta TPD as: TPDs - TPDr (ΔTPD). Patients were categorized as normal (SSS=0-3), mild (SSS=4-8), moderate (SSS=9-12) and severe (SSS≥13) according to the degree of perfusion abnormality based on SSS. Patients with TPD <5%, ≤5<10% and ≥10% were also grouped as normal, mild, and moderate to severely abnormal scan, respectively.

Follow up

All patients were followed up after one year. Patients were classified as those with and without major cardiac events, including cardiac death, non-fatal myocardial infarction, open-heart surgery, abnormal angiographic findings, and unstable angina.

Statistical analysis

Statistical Product and Service Solutions (SPSS) software (version 19) was used for statistical analysis. Comparing different visual MPI results between the event and non-event groups was performed with the chi-square test. To compare quantitative parameters between the event and non-event groups independent t-test was used. The receiver operating characteristic (ROC) curve was applied to evaluate each parameter's prognostic value and compare the corresponding quantitative and semi-quantitative parameters. A P-value of 0.05 was considered the level of significance.

RESULTS

This study evaluated the predictability of semi-quantitative and quantitative methods for major cardiac events in a one-year follow-up.

The major cardiac event was considered one of these items: cardiac death, non-fatal myocardial infarction, open-heart surgery, abnormal angiographic findings, and unstable angina.

This study enrolled a total of 217 participants who met the inclusion criteria. The prevalence of CAD was confirmed in 200 patients after a cardiac catheterization examination. Table 1 summarizes their demographic and clinical characteristics. There were 62 males (31.0%) and 138 females (69.0%) patients, ranging in age from 30 to 86.

Table 1: Clinical characteristics of total patients in this study.

Variable	Status	Number (%)
Gender	Male	62(31)
	Female	138(69)
Chest pain	Typical	32(16)
	Atypical	168(84)
Diabetes Mellitus	Positive	37(18.5)
	Negative	163(81.5)
Hyperlipidemia	Positive	74(37)
	Negative	126(63)
Hypertension	Positive	129(64.5)
	Negative	71(35.5)
Smoking	Positive	36(18)
	Negative	163(81.5)
Obesity	Positive	40(20)
	Negative	160(80)
Family history	Positive	53(26.5)
	Negative	147(73.5)

Table 2 illustrates the percentage of the major cardiac events based on SSS and TPDs scores in CAD patients during a one-year follow-up. The Chi-square test indicated that the major cardiac events were significantly higher in moderate and severe categories based on SSS (P=0.024) and TPDs (P=0.002) scores.

The ROC curve (Figure 1) demonstrates the major cardiac events of the patients studied during one-year follow-up based on SSS and TPDs scores. The difference in AUC (area under the curve) between SSS (0.637) and TPDs (0.632) scores was 0.00504; These indicate that AUC of SSS score and AUC of TPDs score were compatible for predicting major heart events within a year (P = 0.764).

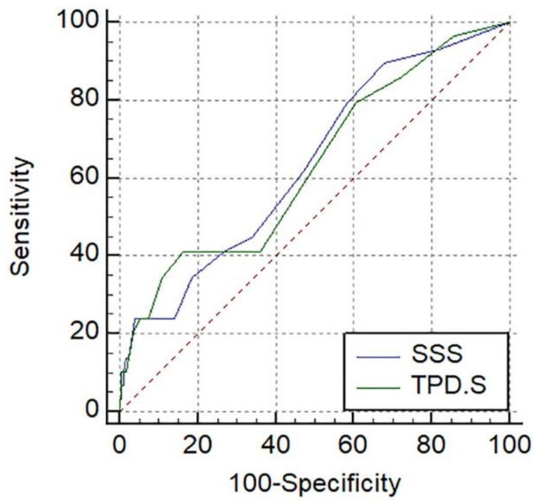

Fig 1. Comparison of ROC curve for prediction of major cardiac events rate after one year based on TPDs and SSS scores.

Figure 2 reveals the comparison of SRS and TPDr scores in predicting major cardiac events by using the ROC curve. The difference level of AUC between TPDr (0.603) and SRS (0.625) was 0.0212, which indicates that AUC of the SRS and AUC of the TPDr were compatible with predicting major cardiac events during one-year follow-up (P = 0.583).

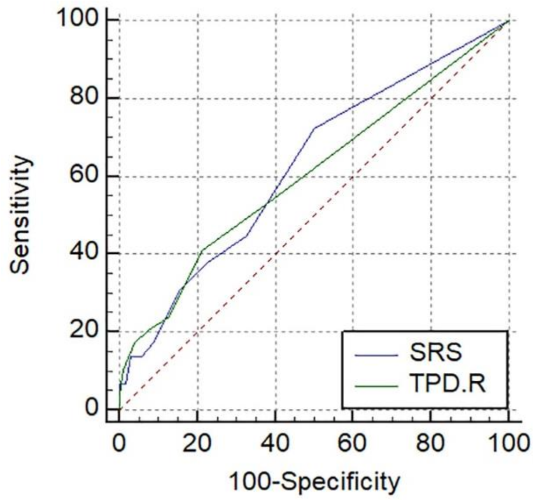

Fig 2. Comparison of ROC curve for prediction of major cardiac events rate after one year based on TPDr and SRS scores.

Figure 3 demonstrates a comparison of ΔTPD and SDS scores in predicting major cardiac events using the ROC curve. The AUC for the SDS score was 0.573, and the ΔTPD was 0.610, and the area difference below the two curves was 0.0377, indicating that both of them were consistent for predicting major heart events (P = 0.118).

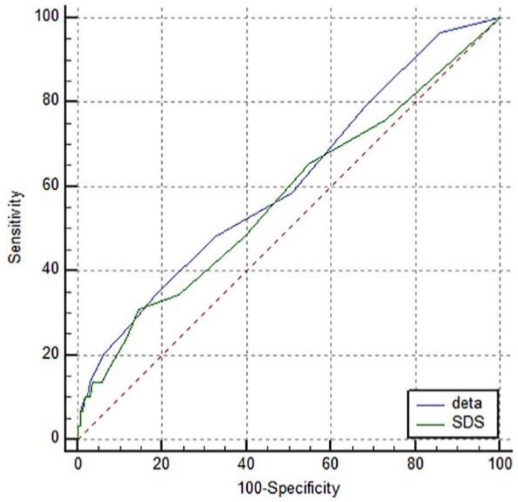

Fig 3. Comparison of ROC curve for prediction of major cardiac events rate after one year based on ΔTPD and SDS scores

The sensitivity and specificity of predicting major cardiac events were assessed by using SDS, ΔTPD scores. The sensitivity and specificity of ΔTPD for predicting consequences are 34.48% and 81.29%, and for SDS are 31.03% and 85.38%, respectively. Cut off point for both indicators is values greater than 4 (Table 3).

Table 3 shows the sensitivity and specificity of predicting major cardiac events by using SSS and TPDs. The rate is 89.66% and 32.16% for SSS and 41.38% and 83.63% for TPDs, separately. Furthermore, the point score's cutoff is greater than 1 for the SSS score and greater than 6 for the TPDs score.

As a final point, Table 3 presents the sensitivity and specificity of predicting major cardiac events based on SRS and TPDr scores, 72.41% and 49.71% for SRS and 41.38% and 78.36% for TPDr, correspondingly. Furthermore, the cutoff point value for the SRS score is greater than 0, and the cutoff point value for TPDr scores is greater than 1.

Table 2: Comparison of visual MPI results between the event and no-event groups.

Variable		Normal	Mild	Moderate	Severe	Total	Pearson Chi-Square	P-value
SSS Score	Event	11(10.9%)	11(14.7%)	3(18.8%)	4(50%)	29(14.5%)	9.428	0.024
	No event	90(89.1%)	64(85.3%)	13(81.3%)	4(50%)	171(85.5%)		
TPD.S Score	Event	17(13.5%)	5(8.6%)	7(43.8%)		29(14.5%)	12.762	0.002
	No event	109(86%)	53(91.4%)	9(56.3%)		171(85.5%)		

Table 3: ROC curve results for prediction of cardiac event rate after 1 year based on the quantitative and semi-quantitative parameters with comparison of AUC between the corresponding parameters.

	Sensitivity	Specificity	AUC	Optimum cut-off	P value
SSS	89.66%	32.16%	0.637	>1	0.764
TPDs	41.38%	83.63%	0.632	>6	
SRS	72.41%	49.71%	0.625	>0	0.583
TPDr	41.38%	78.36%	0.603	>1	
SDS	31.03%	85.38%	0.573	>4	0.118
ΔTPD	34.48%	81.29%	0.610	>4	

DISCUSSION

Myocardial perfusion imaging (MPI) was first used in the 1970s. It quickly became a standard diagnostic technique for CAD disease [9]. Additionally to its diagnostic role, MPI has incremental value in determining prognosis, risk stratification, and therapeutic strategies for these patients [9-10]. Several validated software packages are currently available for automated quantification, distributed by the major suppliers of nuclear medicine imaging equipment [11-12]. MPI combined with SPECT provides diagnostic information on myocardial perfusion. In some clinical circumstances, visual interpretation may be appropriate; however, there are some disadvantages, such as the time-consuming analysis and lack of reproducibility. As a result, the expertise of the observer is crucial. Therefore, the present study aimed to compare MPI SPECT's quantitative and semi-quantitative perfusion parameters' prognostic value.

Comparison of event and nonevent groups in this study revealed no significant difference between the prognostic accuracy of both quantitative and semi-quantitative methods. Several studies have yielded comparable findings [10, 13]. In several studies, a normal MPI through semi-quantitative visual interpretation has been linked to a low risk of potential cardiac events (<1%) [14-15].

ROC curve analysis in the present study also revealed similar prognostic accuracy for the corresponding quantitative and semi-quantitative parameters (AUC of 0.637 and 0.632 for SSS and TPDs, respectively. 0.625, and 0.603 for SRS and TPDr, respectively, and 0.573 and 0.610 for the SDS and ΔTPD, respectively).

In the semi-quantitative visual interpretation, the physician combines all available information, such as patient history, with image data during a typical clinical reading session, comparing the diagnostic precision of visual observers and quantitative analysis challenging. Even when all clinical information was available to the visual readers, equivalence to visual diagnostic performance was observed. On the other hand, Quantitative analysis of myocardial perfusion can rival visual observers' prediction value in detecting CAD. With one study, a standard quantitative approach has been found to achieve performance better than or equivalent to clinical visual assessment in detecting ≥ 50% stenosis as measured by the area under the ROC [16]. Similar results were demonstrated recently in a larger population with blind clinical reads for the blinded expert scoring with and without clinical information [17].

Commercially available software produced various highly specific and reproducible semi-quantitative parameters, compensated for the shortcomings, and improved detection sensitivity, specificity, and accuracy. There have already been comparable studies investigating various semi-quantitative parameters based on various subjects' situations, and the diagnostic thresholds for CAD were varying. For instance, for some people with type 2 diabetes, the TID value for CAD diagnosis has varied [18]. Some other studies have confirmed that these factors were more repeatable than subjective visual interpretation [7, 19, 20].

Based on these results, practically quantitative evaluation of TPD perfusion scan outcomes by using QPS software is a simpler method than a semi-quantitative method to diagnose the perfusion defects in patients with CAD or people who suspected CAD.

In line with the present study's findings, based on a study conducted in 2013 by the Department of Cardiology in Japan, the quantitative method's sensitivity and specificity was about 87%, which was entirely comparable to the semi-quantitative method. Their results indicated that using quantitative methods to analyze cardiac perfusion scans in the Japanese patient population helps coronary artery disease diagnosis [21]. In addition, Xu et al. in 2011 in the united stated of America evaluation of the results of cardiac perfusion scan with the help of the quantitative method by using TPD; They indicated that this method could be replaced with visual-semi-quantitative [7].

TPD is measured automatically by using QPS software. Lower variability translates to better detection of genuine hypo perfusion differences. The reproducibility of quantitative perfusion analysis was studied by repeating stress/rest SPECT acquisitions with the same injection on the same day [16]. However, the semi-quantitative method requires the help of an interpreter. The accuracy of the quantitative TPD method depends on whether the data is normal. Therefore, TPD can be used as a global indicator for CAD diagnosis is obtained from each country's normal data [22].

However, there are some limits in the routine application of perfusion quantification. For the final diagnosis, the expert reader may need to reconcile several quantitative parameters. Imaging objects may make computer analysis sensitive, resulting in false-positive scans. Perfusion measurement may necessitate site-specific normal limits and some manual intervention. To address some of these issues, further research on this software and other related software packages is required.

Due to technical issues, some patients' quantitative data were not included in analyses due to the infeasibility or unreliability of semi-quantitative analysis. In addition, due to inaccessible or altered phone numbers, travel, and other factors, some patients could not be followed up. Better systems and information registries will be required to provide more accurate and accessible data in the future.

CONCLUSION

Total perfusion deficits obtained from QPS software is a useful method for predicting major cardiac events in patients with suspected CAD. Predictive ability of TPD was similar to that of the semi-quantitative method with an expert interpreter's help. Moreover, this method can be helpful for the diagnosis of CAD and therapeutic evaluation of patients.

Acknowledgement

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REFERENCES

1. Al-Mallah MH, Sakr S, Al-Qunaibet A. Cardiorespiratory fitness and cardiovascular disease prevention: an update. Curr Atheroscler Rep. 2018;20(1):1.
2. Joseph P, Leong D, McKee M, Anand SS, Schwalm J-D, Teo K, Mente A, Yusuf S. Reducing the global burden of cardiovascular disease, part 1: the epidemiology and risk factors. Circ Res. 2017;121(6):677-94.
3. Stanner S, Coe S, Frayn KN. Cardiovascular disease: diet, nutrition and emerging risk factors. John Wiley & Sons; 2018.
4. Ajay VS, Watkins DA, Prabhakaran D. Relationships among major risk factors and the burden of cardiovascular diseases, diabetes, and chronic lung disease. In: Cardiovascular, Respiratory, and Related Disorders. 3rd edition. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2017.
5. Kazemi T, GhR SZ. The proportion of CVD from total death in Birjand, 2002-03. J Qazvin Univ Med Sci. 2005;33:73-6.
6. Berman DS, Kang X, Gransar H, Gerlach J, Friedman JD, Hayes SW, Thomson LE, Hachamovitch R, Shaw LJ, Slomka PJ, De Yang L. Quantitative assessment of myocardial perfusion abnormality on SPECT myocardial perfusion imaging is more reproducible than expert visual analysis. J Nucl Cardiol. 2009;16(1):45.
7. Xu Y, Nakazato R, Hayes S, Hachamovitch R, Cheng VY, Gransar H, Miranda-Peats R, Hyun M, Shaw LJ, Friedman J, Germano G. Prognostic value of automated vs visual analysis for adenosine stress myocardial perfusion SPECT in patients without prior coronary artery disease: A case-control study. J Nucl Cardiol. 2011;18(6):1003-9.
8. Yoda S, Nakanishi K, Tano A, Hori Y, Suzuki Y, Matsumoto N, Hirayama A. Validation of automated quantification of nuclear cardiology in Japanese patients using total perfusion deficits: comparison with visual assessment. J Cardiol. 2014;63(5):350-7.
9. Underwood S, Godman B, Salyani S, Ogle J, Ell P. Economics of myocardial perfusion imaging in Europe—the EMPIRE Study. Eur Heart J. 1999 Jan;20(2):157-66.
10. Chavoshi M, Fard-Esfahani A, Fallahi B, Emami-Ardekani A, Beiki D, Hassanzadeh-Rad A, Eftekhari M. Assessment of prognostic value of semiquantitative parameters on gated single photon emission computed tomography myocardial perfusion scintigraphy in a large middle eastern population. Indian J Nucl Med. Jul-Sep 2015;30(3):233-8
11. 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(4):433-54.
12. Patton JA, Slomka PJ, Germano G, Berman DS. Recent technologic advances in nuclear cardiology. J Nucl Cardiol. 2007;14(4):501-13.
13. Soman P, Parsons A, Lahiri N, Lahiri A. The prognostic value of a normal Tc-99m sestamibi SPECT study in suspected coronary artery disease. J Nucl Cardiol. 1999;6(3):252-6.
14. Metz LD, Beattie M, Hom R, Redberg RF, Grady D, Fleischmann KE. The prognostic value of normal exercise myocardial perfusion imaging and exercise echocardiography: a meta-analysis. J Am Coll Cardiol. 2007;49(2):227-37.
15. Shaw LJ, Hendel RC, Heller GV, Borges-Neto S, Cerqueira M, Berman DS. Prognostic estimation of coronary artery disease risk with resting perfusion abnormalities and stress ischemia on myocardial perfusion SPECT. J Nucl Cardiol. 2008;15(6):762-73.
16. Slomka P, Xu Y, Berman D, Germano G. Quantitative analysis of perfusion studies: strengths and pitfalls. J Nucl Cardiol. 2012;19(2):338-46.
17. Arsanjani R, Xu Y, Hayes SW, Fish M, Lemley M, Gerlach J, Dorbala S, Berman DS, Germano G, Slomka P. 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;54(2):221-8.
18. Petretta M, Acampa W, Daniele S, Petretta MP, Nappi C, Assante R, Zampella E, Costanzo P, Perrone-Filardi P, Cuocolo A. Transient ischemic dilation in SPECT myocardial perfusion imaging for prediction of severe coronary artery disease in diabetic patients. J Nucl Cardiol. 2013;20(1):45-52.
19. Berman DS, Kang X, Gransar H, Gerlach J, Friedman JD, Hayes SW, Thomson LE, Hachamovitch R, Shaw LJ, Slomka PJ, De Yang L. Quantitative assessment of myocardial perfusion abnormality on SPECT myocardial perfusion imaging is more reproducible than expert visual analysis. J Nucl Cardiol. 2009;16(1):45-53.
20. Chang C-C, Yang M-H, Liu C-T, Chu H-L, Lin C-Y, Yen W-J, Chung CY, Ho SY, Tyan YC. Relationship between semi-quantitative parameters of thallium-201 myocardial perfusion imaging and coronary artery disease. Diagnostics. 2020;10(10):772.
21. Yoda S, Nakanishi K, Tano A, Hori Y, Suzuki Y, Matsumoto N, Hirayama A. Usefulness of automated assessment of nuclear cardiology for prediction of major cardiac events in Japanese patients with known or suspected coronary artery disease: comparison with conventional visual assessment in a large-scale prognostic study. J Nucl Cardiol. 2014;64(5):395-400.
22. Yoda S, Nakanishi K, Tano A, Hori Y, Suzuki Y, Matsumoto N, Hirayama A. Diagnostic value of automated quantification of nuclear cardiology in Japanese patients with single vessel coronary artery disease: comparison between Japanese and American normal databases. J Cardiol.2013;62(4):224-9.