Abstract

Objective. An iterative reconstruction method in combination with resolution recovery, attenuation and scatter corrections (IR-RASC) can improve image quality. It, however, is undetermined whether this technique can improve the detection of coronary artery disease (CAD) when automated quantitative analysis is used. This study evaluated diagnostic values of IR-RASC in combination with automated quantitative analysis in stress myocardial perfusion imaging (MPI) in the CAD detection.

Methods. This study enrolled consecutive 64 patients (mean age 66.2 ± 17.3 years, 39 males) who had undergone both ^{99m}Tc-labeled tetrofosmin stress MPI and coronary angiography within 3 months. Stress MPI abnormalities quantified as summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS) by Heart Risk View-S (HRV-S) and Quantitative Perfusion SPECT (QPS) softwares using IR-RASC images were compared with those by using conventional filtered back-projection method (FBP) images and angiographic findings.

Results. Based on expert visual assessment, SSS and SRS by HRV-S/QPS softwares with IR-RASC were significantly lower than those by HRV-S/QPS softwares with FBP at mid- and basal left ventricular segments. Receiver-operating characteristics analysis showed that areas under the curve assessed by HRV-S (0.687) and QPS (0.678) with IR-RASC were nearly identical to those (0.717 to 0.724) by expert assessment with FBP, and were significantly (p<0.05) greater than those by HRV-S (0.505) and QPS (0.522) with FBP. When HRV-S was used, the specificity and diagnostic accuracy of IR-RASC in the CAD detection were significantly greater than those of FBP: 90.3% versus 51.6%, p<0.0001, and 79.7% versus 54.7%, p=0.0027, respectively. Likewise, when QPS was used, the specificity and diagnostic accuracy of IR-RASC in the CAD detection were significantly greater than those of FBP: 80.6% versus 41.9%, p<0.0001, and 78.1% versus 51.6%, p=0.0018, respectively. There, however, was no significant differences in sensitivity between IR-RASC and FBP images.

Conclusions. IR-RASC can improve diagnostic accuracy of the CAD detection using an automated scoring system compared to FBP, by reducing false positivity due to artefactual appearance.

Keywords: Automated quantitation・Iterative reconstruction・Resolution recovery・

Attenuation correction・Scatter correction

Introduction

Stress myocardial perfusion single photon emission computed tomography (SPECT) has robust clinical evidence to show clinical efficacies not only in the noninvasive detection of coronary artery disease (CAD) but also in the risk-stratification of patients with known or suspected CAD on future cardiovascular events [1-6]. Semi-quantitative visual analysis (a 5-point, 17-segment model) has been widely utilized in the assessment of stress myocardial SPECT imaging, but requires experienced experts to maintain a reliable diagnostic accuracy and a high reproducibility by minimizing inter- and intra-observer errors and by precisely identifying image artifacts. Instead of visual quantitative analysis, there are several softwares developed for automated quantification of myocardial perfusion abnormality and cardiac function [7-10]. These softwares are basically applied for SPECT images reconstructed by a conventional filtered back-projection method (FBP). FBP, however, has substantial limitations due to attenuation artifacts and effects from an increased activity of adjacent organs, reducing diagnostic reliability and clinical application of computerized quantitative analysis. Iterative reconstruction, such as ordered-subset expectation maximization (OSEM), is recently available for the improvement in signal-to-noise ratio of myocardial perfusion count and for the reduction in artifacts due to reconstruction and radiation from liver or gall bladder [11, 12]. This method is likely to improve visual assessment of CAD in combination with resolution recovery, attenuation and scatter corrections compared to FBP [13, 14]. It, however, is not determined whether an iterative reconstruction method in combination with resolution recovery, attenuation and scatter corrections (IR-RASC) can improve CAD detection when automated quantitative analysis is applied for stress SPECT image. This study was designed to clarify diagnostic reliability of IR-RASC when automated quantitative scoring system is applied to stress myocardial perfusion SPECT for the detection of CAD by comparing with expert visual assessment using FBP image without any correction.

Materials and Methods

Subjects

The study population consisted of consecutive 64 patients (mean age, 66.2 ± 17.3 years; 39 males and 25 females) who had undergone both stress ^{99m}Tc-tetrofosmin SPECT and coronary angiography (CAG) within 3 months from May, 2012 to December, 2015 at the nuclear medicine laboratory of the Sapporo Medical University Hospital, Sapporo, Japan. The institutional ethics committee of Sapporo Medical University Hospital approved the study protocol. The exclusion criteria were as followed; 1) prior myocardial infarction, 2) a history of coronary revascularization, 3) multi-vessel CAD and 4) cardiomyopathy.

Stress-rest myocardial perfusion imaging

Stress-rest myocardial SPECT imaging was performed using ^{99m}Tc-tetrofosmin with 296 MBq for a stress study and 740 MBq for a rest study. A dual-headed SPECT system equipped with low-energy high-resolution collimator (Discovery NM/CT 670: SPECT/CT scanner, GE Healthcare, Milwaukee, WI) was used for data acquisition with a 180-degree acquisition. A photopeak window of ^{99m}Tc was set as a 15 % energy window centered at 140 keV, and a high and low sub-window for scatter correction

(SC) was set as a 7 % of photopeak window. The acquisition pixel size was a 6.6 mm for a 64 x 64 matrix. We acquired a low-dose computed tomography (CT) image for attenuation correction (AC) using a 16-deteor row CT on the SPECT/CT scanner. Tube voltage and effective mAs for AC CT were 120 kVp and 10 mAs, respectively. We used two reconstruction methods, FBP and IR-RASC. RASC algorithm was not incorporated into the conventional FBP processing. An iterative reconstruction method used OSEM with 12 iterations and 10 subsets. Reconstructed stress and rest images were smoothed by use of a 3-dimensional Butterworth low pass filter with a critical frequency of 0.4 Nyquist with an order of 10 and a critical frequency of 0.5 Nyquist with an order of 10, respectively.

Automated quantitation of myocardial perfusion abnormality

Automated quantification of myocardial perfusion abnormality was performed using Heart Risk View-S (HRV-S, Nihon Medi-Physics Co Ltd, Tokyo, Japan) mounted on AZE Virtual Place Hayabusa (AZE Co Ltd, Tokyo, Japan) and Quantitative Perfusion SPECT (QPS) software (Cedars-Sinai Medical Center, USA) for the evaluation of applicability of IR-RASC. Based on the 17-segment, 5-point scoring model recommended by Cardiac Imaging Committee of the American Heart Association and the American Society of Nuclear Cardiology (ASNC) guidelines [15], HRV-S automatically measured a mean percent count at each 17-segment, scored with a 5-point method from normal (0) to absent (4), then calculated summed stress score (SSS), summed rest score (SRS) and summed difference (SDS). The threshold of a mean percent uptake for the 5-point scoring system each segment was determined using the gender-, tracer- and acquisition angle-based database developed by the Japanese Society of Nuclear Medicine working group (JSNM WG) [16] (Table 1). Regional SSS, SRS and SDS were also calculated separately at apical, mid- and basal left ventricular areas to evaluate effect of each reconstruction method on automated scoring data.

Visual assessment and CAD definition

Visual interpretation of myocardial perfusion SPECT image reconstructed by FBP was performed using a 5-point, 17-segment model by two nuclear cardiology experts (A.H. and N.Y.) blinded to clinical data as follows: 0, normal; 1, mildly reduced; 2, moderately reduced; 3, severely reduced; and 4, absent. SSS, SRS and SDS were calculated. CAD was defined angiographically as a diameter stenosis of ≥50% at any of 3 main coronary arteries or their major branches by visual assessment [17]. Scintigraphic CAD was defined as SDS ≥2 in stress myocardial SPECT imaging, because the pilot studies reporting a diagnostic capacity of automated quantitative program software have proposed SDS=2 as the optimal cut-off value for identifying angiographical CAD [18, 19]. A true positive was defined angiographically as a diameter stenosis of ≥50% and SDS ≥2 in stress myocardial SPECT imaging. A true negative was defined angiographically as a diameter stenosis of <50% and SDS <2 in stress myocardial SPECT imaging.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation and compared using the paired two-tailed Student's t test. Multiple comparisons were analyzed using the Scheffe test. Agreement among summed scores between two methods was evaluated by Pearson's correlation coefficient for linear regression. The diagnostic accuracy of CAD was evaluated using receiver-operating characteristics (ROC) curve analysis and area under the curve (AUC) and Pearson's Chi-square test. A one-way ANOVA and post-hoc analysis using Scheffe test were used to test for statistically significant differences between two AUCs from the six different ROC curves. A p value <0.05 was considered statistically significant. These analyses were performed by using MedCalc software (MedCalc software, Mariakerte, Belgium, 2009).

Results

Angiographic CAD was identified in 33 (51.5%) of 64 patients; 15 lesions in left anterior descending artery, 11 in left circumflex artery and 7 in right coronary artery. There was no significant difference in clinical backgrounds between CAD and non-CAD patients (Table 2). When FBP images were used, SSS and SRS assessed by HRV-S and QPS were significantly greater than those assessed by visual interpretation of Readers 1 and 2 (Table 3), particularly at mid- and basal left ventricular areas (Figure 1). When IR-RASC images were used, however, there was no significant difference in SSS or SRS between the automated analyses (HRV-S and QPS) and the expert visual assessment (Table 3). SSS, SRS and SDS more closely correlated between expert visual assessment and automated analyses when IR-RASC images were used for the HRV-S and QPS compared to those when FBP images were used (Figures 2-4).

Receiver-operating characteristics analysis showed that AUCs assessed by HRV-S (0.687) and QPS (0.678) with IR-RASC were nearly identical to those (0.717 to 0.724) by visual analysis (Readers 1 and 2) with FBP, and were significantly ($p<0.05$) greater than those by HRV-S (0.505) and QPS (0.522) with FBP (Figure 5). When HRV-S was used, the specificity and diagnostic accuracy of IR-RASC in the CAD detection were significantly greater than those of FBP: 90.3% versus 51.6%, $p<0.0001$ and 79.7% versus 54.7%, $p=0.0027$, respectively (Table 4). Likewise, when QPS was used, the specificity and diagnostic accuracy of IR-RASC in the CAD detection were significantly greater than those of FBP: 80.6% versus 41.9%, $p<0.0001$ and 78.1% versus 51.6%, $p=0.0018$, respectively. There, however, was no significant difference in sensitivity between IR-RASC and FBP irrespective of softwares used. These diagnostic values of IR-RASC with HRV-S or QPS were nearly identical to those of visual assessment; 66.7% for sensitivity, 87.1% for specificity and 76.6% for accuracy.

Case presentation

Figure 6 shows typical stress and resting SPECT images reconstructed by FBP and IR-RASC in a normal case. Because of artefactual appearance at anterobasal, inferobasal and lateral segments of FBP images, SSS, SRS and SDS were overestimated by HRV-S and visual analysis, but were reasonably estimated by using IR-RASC. In a CAD patient with a 60% stenosis of left circumflex coronary artery, SSS, SRS and SDS underestimated by HRV-S using FBP images were more precisely estimated by visual analysis and HRV-S using IR-RASC images (Figure 7).

Discussion

The present study clearly demonstrated the diagnostic superiority of IR-RASC to FBP in stress myocardial perfusion SPECT imaging to which automated quantitative assessment using HRV-S and QPS is applied. The presented method using IR-RASC can reduce overestimation of artefactual perfusion abnormalities particularly at mid- and basal left ventricular areas, contributing to improvement in the specificity of detection of CAD. Furthermore, the overall diagnostic accuracy of the computer-assisted scoring systems using IR-RASC is nearly identical to expert visual assessment.

Conventional automated scoring programs are based on self-normalized counts as relative percent uptake and, therefore, tend to overestimate artefactual perfusion abnormality inherent in SPECT imaging due to motion artifacts, attenuation artifacts due to diaphragm or breast, selection error of basal segments and reconstruction artifacts by FBP [9, 19]. Recently, a software package called Heart Score View (HSV; version 1.5) (Nihon Medi-Physics, Japan), previous version of HRV-S, was developed and widely used in Japan. The application of HSV software to stress myocardial perfusion SEPCT studies with ^{99m}Tc-labeled tracers can improve specificity (80-88%) and accuracy (75-81%), rather than sensitivity (71-75%), in the detection of CAD [7,8]. In these studies, however, the automated computerized analysis was used complimentarily when a low count-image or artefactual image makes visual assessment difficult. IR-RASC in combination with automated scorning system improved the specificity in the CAD detection significantly by reducing SSS and SRS overestimated at anterobasal, inferobasal and lateral segments in FBP images in this study. IR-RASC images can reduce spatial heterogeneity of SPECT counts and artefactual abnormality and more precisely identify left ventricular wall contour when compared to FBP images. This is because iterative reconstructions with resolution recovery and noise reduction algorithms can significantly improve perfusion defect contrast and spatial resolution [20]. Thus, IR-RASC can improve the quantitative assessment using HRV-S and QPS as a full automated scoring system when compared to FBP.

Despite a robust evidence of quantitative visual analysis of stress perfusion SPECT imaging, visual assessment requires nuclear cardiology training, experience and expertise to reduce inter- and intra-observer errors among physicians with less experience [21]. High-image quality and reliable automated quantitative analysis with IR-RASC can contribute not only to better diagnostic performance, high interpretive reproducibility and time-saving in a routine clinical practice of stress myocardial perfusion study with ^{99m}Tc-labeled tracers but also to education of physicians and nuclear cardiology staff with a wide range of training and experience in distinguishing various sorts of artifacts from true myocardial perfusion abnormality or ischemia.

The presented study includes limitations to be resolved in a future study. Because of a lack of a normal database incorporated into resolution recovery, attenuation and scatter corrections used here, automated quantification of myocardial perfusion abnormality was performed using the conventional database created without any correction. In this study, FBP images without any correction were used to compare with IR-RASC images created by full corrections available at present time. Therefore, this study showed no data derived from each correction or combinations rather than the whole process of IR-RASC. Nevertheless, Narayanan MV, et al [13] showed incremental improvements in the overall detection of CAD by adding attenuation correction, scatter correction and resolution compensation to OSEM in the visual assessment of FBP reconstructed images. Finally, a larger-scale study is required to clarify prognostic values of automated quantitative system using IR-RASC as shown by multicenter studies using automated quantitative analysis with FBP [10, 22].

Conclusion

IR-RASC can improve diagnostic accuracy of stress myocardial perfusion imaging using an automated scoring system such as HRV-S and QPS in the CAD detection when compared to FBP, by reducing false positivity due to artefactual appearance.

Conflict of interest The authors have declared no conflicts of interest.

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Figure legends

Figure 1 Comparison of regional summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS) at apical, mid- and basal left ventricular areas between automated quantitative analysis (HRV-S and QPS) using FBP or IR-RASC images and expert (Readers 1 and 2) visual interpretation using FBP images.

HRV-S: Heart Risk View-S, QPS: Quantitative Perfusion SPECT, FBP: filtered back-projection method, IR-RASC: iterative reconstruction method in combination with resolution recovery, attenuation and scatter corrections

*P<0.05 versus HRV-S with FBP, **P<0.05 versus QPS with FBP

Figure 2 Correlations of summed stress score (SSS) between automated quantitative analysis (HRV-S and QPS) with FBP/IR-RASC and visual (Readers 1 and 2) interpretation with FBP.

Please see the abbreviations in Figure 1.

Figure 3 Correlations of summed rest score (SRS) between automated quantitative analysis (HRV-S and QPS) with FBP/IR-RASC and visual (Readers 1 and 2) interpretation with FBP.

Please see the abbreviations in Figure 1.

Figure 4 Correlations of summed difference score (SDS) between automated quantitative analysis (HRV-S and QPS) with FBP/IR-RASC and visual (Readers 1 and

2) interpretation with FBP.

Please see the abbreviations in Figure 1.

Figure 5 Receiver operating curve analysis of the diagnostic accuracy of HRV-S with FBP or IR-RASC, QPS with FBP or IR-RASC and expert (Readers 1 and 2) visual interpretation with FBP in the detection of coronary artery disease.

Please see the abbreviations in Figure 1.

Figure 6 FBP images (left panels) from a patient without a coronary stenosis overestimate scores by HRV-S and expert analysis due to artefactual perfusion abnormalities at anterobasal, inferobasal and lateral segments, but IR-RASC images (right panels) are significantly improved, contributing to more appropriate assessment of summed stress score (SSS), summed rest score (SRS) and summed difference (SDS).

Please see the abbreviations in Figure 1.

Figure 7 FBP images (left panels) from a patient with a 60% stenosis of left circumflex coronary artery underestimated lateral-wall perfusion abnormality but HRV-S using IR-RASC images (right panels) precisely score the perfusion abnormality, resulting in increases in summed stress score (SSS) and summed difference (SDS).

Please see the abbreviations in Figure 1.