Journal of Cardiology 62 (2013) 224–229

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Diagnostic value of automated quantification of nuclear cardiology in Japanese patients with single vessel coronary artery disease: Comparison between Japanese and American normal databases

Shunichi Yoda (MD)*, Kanae Nakanishi (MD), Ayako Tano (MD), Yusuke Hori (MD), Yasuyuki Suzuki (MD), Naoya Matsumoto (MD, FJCC), Atsushi Hirayama (MD, FJCC)

Department of Cardiology, Nihon University School of Medicine, Tokyo, Japan

ARTICLE INFO

Article history:
Received 21 December 2012
Received in revised form 12 April 2013
Accepted 17 April 2013
Available online 31 May 2013

Keywords:
Coronary artery disease
Coronary vessels
Computer-assisted imaging processing
Radionuclide imaging
Gender-related risk factors

ABSTRACT

Background: The Japanese diagnostic assessment of nuclear cardiology has usually been based on semi-quantitative visual analyses but not on automated quantification with a total perfusion deficit (TPD). We, therefore, aimed to determine whether automated TPD quantification is useful to detect coronary artery disease (CAD) in Japanese patients in comparison with conventional visual segmental analysis, and to compare results from the automated assessment between the Japanese and American normal databases (NDBs).

Methods: Patients with suspected CAD underwent rest ^{201}Tl and stress ^{99m}Tc-tetrofosmin myocardial perfusion single photon emission computed tomography (SPECT) and coronary angiography within three months. The TPD was automatically derived from the SPECT image through quantitative perfusion SPECT software with the Japanese and American NDBs. The visual summed stress scores (SSS) were estimated with the 5-point visual scoring model for 20 segments of SPECT images. An abnormal criteria for the stress TPD and SSS were defined as ≥5% and ≥4, respectively.

Results: Detection sensitivity of CAD was 87% with the stress TPD score derived from the Japanese NDB and 85% with the SSS in visual analysis. In contrast, the detection sensitivity with the stress TPD score derived from the American NDB was 75%, which was significantly lower than that with the Japanese TPD ($p = 0.0004$). Specificity of the automated Japanese TPD assessment was similar to that of the visual SSS assessment (87% vs. 80%). Thus, sensitivity and specificity of the automated quantitative assessment based on the TPD scores derived from the Japanese NDB were consistent with that of visual quantification based on the segmental defect scores.

Conclusion: The automated quantitative assessment with the Japanese NDB is useful for the detection of CAD when experts in visual interpretation of a myocardial perfusion SPECT image were absent in a clinical setting.

Introduction

Gated myocardial perfusion single photon emission computed tomography (SPECT) is a pivotal technique in nuclear cardiology to provide imaging data, which are useful for consideration of myocardial blood flow and viability, using radiopharmaceutical injection. To interpret the imaging data and to secure quality control, Germano et al. [1] developed a quantitative perfusion SPECT (QPS) algorithm, which allowed automated quantitative assessment of a defect on a polar map. The QPS software was confirmed to be highly sensitive and specific for the detection and localization of coronary artery disease (CAD) [2], and thereafter, the software has been used worldwide as the standard algorithm. The QPS software can estimate various ischemic parameters, including summed stress score (SSS) and summed rest score (SRS), by comparisons between patient's data and normal limits. However, the estimation process includes visual quantitative assessment by an experienced observer because the normal limits fail to provide all-purpose thresholds. Therefore, regional abnormality thresholds should be determined for each quantification method and each population studied.

Slomka et al. [3] proposed a total perfusion deficit (TPD), as a new objective parameter, which represented both severity and extent of a defect in comparison with normal databases (NDBs) created based on American myocardial perfusion imaging data, and reported that the TPD could achieve performance better than or equivalent to visual quantification based on per-segment visual

* Corresponding author at: Department of Cardiology, Nihon University School of Medicine, 30-1 Oyaguchi-Kamicho, Itabashi-Ku, Tokyo 173-8610, Japan.
Tel.: +81 3 3972 8111; fax: +81 3 3972 1098.
E-mail address: masteryoda@mf.point.ne.jp (S. Yoda).

0914-5087/$ – see front matter © 2013 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jjcc.2013.04.001

optimization of abnormality thresholds. In addition, automated quantitative assessment with the TPD was confirmed to provide highly correlated results with visual interpretation by three experts and to be more reproducible than the visual quantitative assessment for defect extent [4].

The automated quantitative assessment with the TPD has been treated as a reliable technique detecting CAD in the multicenter trial [5] and the American Society of Nuclear Cardiology (ASNC) imaging guideline 2010 for SPECT [6].

On the other hand, the Japanese diagnostic assessment of nuclear cardiology has usually been based on a semi-quantitative visual analysis but not on automated quantification with the TPD. A reason for this is that the automated quantitative assessment requires a validated NDB for myocardial perfusion. We had no validated Japanese NDBs when the automated quantification with the TPD was established in the USA. Also, it was unclear whether the American NDBs could be applied to Japanese nuclear cardiology. As for the normal limit mentioned above, NDBs should be created in consideration of a procedure of SPECT including stress and rest acquisition protocols, a sort and dosing schedule of radiopharmaceuticals and 180° or 360° acquisition. In recent years, the Japanese Society of Nuclear Medicine developed a Japanese NDB for myocardial perfusion images obtained from subjects with a low-likelihood of cardiac disease [7]. However, there are no reports that diagnostic sensitivity and specificity of CAD based on the TPD were compared between NDBs from different populations.

We have been investigating the diagnostic value of automated quantitative assessment using the TPD that has not yet become popular in Japan. The objectives of the present study were to retrospectively determine whether automated quantitative assessment with the TPD derived from the Japanese NDB is useful to detect CAD in Japanese patients in comparison with conventional segmental defect scores estimated by visual quantitative assessment. In addition, the automated quantitative assessment with Japanese TPD was compared with that based on the TPD derived from the American NDB to clarify whether diagnostic results from the assessments are different between the two NDBs.

Materials and methods

The institutional review board of Nihon University Itabashi Hospital approved this study, which proceeded in accordance with the ethical standards established in the 1964 Declaration of Helsinki. All study participants provided written informed consent prior to inclusion in this study.

Patient population

The study population comprised 165 consecutive patients with suspected CAD who underwent rest ^{201}Tl and stress ^{99m}Tc-tetrofosmin myocardial perfusion SPECT [8–11] and coronary angiography within three months. We excluded patients who had multi-vessel CAD, those who had a history of myocardial infarction, those who underwent any type of coronary revascularization, and those who developed non-ischemic cardiomyopathy or valvular heart disease. The assessment was performed in only patients having one-vessel CAD because of strict assessment of differences between Japanese and American NDBs based on correct sensitivity and specificity by coronary artery territory.

Japanese and American NDBs

The Japanese NDB used was one developed by the Japanese Society of Nuclear Medicine [7], which is based on exercise-rest myocardial perfusion images accumulated from 80 subjects with a low likelihood of cardiac disease. The American NDB used was one distributed with the QPS software [3], which was previously validated by Cedars-Sinai Medical Center (Los Angeles, CA, USA), and was created from 40 male and 40 female subjects with a low likelihood of CAD.

Electrocardiography-gated dual-isotope myocardial perfusion SPECT

The procedure of rest ^{201}Tl and stress ^{99m}Tc-tetrofosmin electrocardiography (ECG)-gated myocardial perfusion SPECT was performed as a protocol previously reported [8–11]. All patients received an intravenous (i.v.) injection of ^{201}Tl (111 MBq) and sixteen-frame gated SPECT image was initiated 10 min after injection during rest. Then an i.v. injection of ^{99m}Tc-tetrofosmin (740 MBq) was performed under stress induced by ergometer exercise in 26% of the patients or by adenosine triphosphate in 74% of them. Sixteen-frame gated SPECT image was initiated 30 min after exercise or 30–60 min after adenosine stress. No attenuation or scatter correction was used. Twelve-lead ECG was monitored continuously during stress tests. Heart rate and blood pressure were recorded at baseline and every minute for at least 3 min after stress.

Coronary angiography

Coronary angiography (CAG) was performed within three months after the SPECT imaging. All coronary angiograms were visually interpreted by experienced cardiologists who were given no previous notice of the SPECT data. A stenosis with 75% or greater narrowing of the luminal diameter, which was considered significant, was used as a gold standard for the detection of CAD.

Automated perfusion analysis

The projection data over 360° were obtained with 64 × 64 matrices and a circular orbit. A triple-detector SPECT system equipped with low-energy high-resolution collimators was used (Toshiba, GCA9300A, Tokyo, Japan). The quantitative perfusion variable used was a TPD, which is a parameter representing both defect extent and severity of myocardial abnormality, was automatically computed. TPD scores were calculated as the percentage of the total surface area of the left ventricle below the predefined uniform average deviation threshold using QPS software. The TPD scores were measured at stress and rest, and ischemic TPD was calculated from the difference between the stress and rest TPD scores (stress TPD minus rest TPD). An abnormal criterion for the stress TPD was defined as 5% or more [5].

Visual perfusion analysis

The SPECT images were divided into 20 segments on three short-axis (distal, mid, basal) and one vertical long-axis (mid) slices, and the tracer uptake of each segment was visually scored using a 5-point scale (0: normal; 1: slight reduction of uptake; 2: moderate reduction of uptake; 3: severe reduction of uptake; and 4: absence of uptake). The sum total of the scores of 20 segments in the stress and rest images provided the summed stress score (SSS) and the summed rest score (SRS), respectively. The summed difference score (SDS) was calculated as the difference between the SSS and SRS. An abnormal criterion for the SSS was defined as 4 or more [4]. Cohen's kappa (κ), which was calculated to determine the inter-observer variability for the perfusion score, was 0.92, indicating very good reproducibility.

Sixteen-frame quantitative gated SPECT data were analyzed using QGS^{TM} software (Cedars-Sinai Medical Center) to calculate left ventricular ejection fraction (LVEF, %), end-diastolic volume