Journal of Cardiology 65 (2015) 278–284

Contents lists available at ScienceDirect

Journal of Cardiology

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

Original article

Myocardial ischemic reduction evidenced by gated myocardial perfusion imaging after treatment results in good prognosis in patients with coronary artery disease

Yusuke Hori (MD), Shunichi Yoda (MD)*, Kanae Nakanishi (MD), Ayako Tano (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 13 March 2014
Received in revised form 27 June 2014
Accepted 30 June 2014
Available online 28 July 2014

Keywords:
Radionuclide imaging
Myocardial ischemic reduction
Revascularization
Prognosis
Coronary artery disease

ABSTRACT

Background: There are no nuclear cardiology reports indicating the prediction of prognosis based on ischemic reduction after revascularization in Japanese patients with coronary artery disease (CAD). We aimed to evaluate quantitatively ischemia using myocardial perfusion single photon emission computed tomography (SPECT) before and after treatment such as revascularization and to determine a relationship between the ischemic reduction and the incidence of major cardiac events (MCEs) after the treatment in patients with CAD.
Methods: We retrospectively investigated 513 patients who underwent rest ^{201}Tl and stress ^{99m}Tc-tetrofosmin myocardial perfusion SPECT between October 2004 and March 2011 and who had a significant stenosis with 75% or greater narrowing of the coronary arterial diameter detected by coronary angiography performed after confirmation of $\geq$5% ischemia with SPECT. The patients underwent the treatment including revascularization and medication and thereafter were re-evaluated with SPECT during a chronic phase and followed up to confirm prognosis for $\geq$1 year. The follow-up period was 33.4 ± 16.4 months. The endpoint was the incidence of the MCEs consisting of cardiac death, non-fatal myocardial infarction, and unstable angina pectoris.
Results: During the follow-up, 45 patients experienced MCEs comprising cardiac death ($n = 13$), non-fatal myocardial infarction ($n = 3$), and unstable angina pectoris ($n = 29$). The multivariate Cox proportional hazards regression model analysis for the risk of the MCEs showed the changes in the summed difference score % ($p = 0.0102$) and the stress left ventricular ejection fraction after the treatment ($p = 0.0146$) as significant independent variables. The incidence of the MCEs significantly decreased in the patients with $\geq$5% ischemic reduction than in the patients without $\geq$5% ischemic reduction and in the patients without residual ischemia than in the patients with the residual ischemia.
Conclusion: Myocardial ischemic reduction detected by nuclear cardiology leads to a decrease in MCE rates after treatment in Japanese patients with CAD.

Introduction

Myocardial perfusion single photon emission computed tomography (SPECT) has been well recognized as a useful imaging method for the prediction of future cardiac events in patients with known or suspected coronary artery disease (CAD) since the reports of Hachamovitch et al. [1,2].

In Japan, myocardial perfusion SPECT has also commonly been used to predict cardiac events in patients with CAD. Risk stratification of cardiac events by nuclear cardiology has been demonstrated in some large-scale prognostic studies including the multicenter prospective Japanese Assessment of Cardiac Events and Survival Study in patients with ischemic heart disease (J-ACCESS) [3], in asymptomatic patients with type 2 diabetes (J-ACCESS 2) [4], and patients with chronic kidney disease (J-ACCESS 3) [5], and another single-center large-scale prospective study [6]. In those studies, patients who underwent revascularization within 60 days after baseline SPECT were excluded from assessment and the prognosis of patients with CAD was predicted based on the baseline SPECT. However, it is also

* 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).

http://dx.doi.org/10.1016/j.jjcc.2014.06.015
0914-5087/

clinically important to evaluate cardiac event rates after revascularization.

The COURAGE (clinical outcomes utilizing revascularization and aggressive drug evaluation) trial [7] was conducted to compare cardiac event rates between patients with stable angina pectoris undergoing percutaneous coronary intervention (PCI) with optimal medical treatment and those receiving optimal medical treatment alone in the USA. The incidence of cardiac death and non-fatal myocardial infarction (MI) was 19.0% in the patients with PCI and 18.5% in those without PCI, and long-term prognosis was similar between the two patient populations. However, a nuclear sub-study [8] of the COURAGE trial in 314 patients who underwent SPECT before and after PCI provided interesting data, namely, significant ischemic reduction was observed in patients treated with optimal medication adding PCI. Prognosis was more favorable in the patients with at least 5% ischemic reduction after PCI than without at least 5% ischemic reduction after PCI and also with residual ischemia approaching zero.

Assessment of myocardial ischemia with SPECT before and after PCI is considered to be useful for the prediction of prognosis after PCI on the basis of the results from the nuclear sub-study of the COURAGE trial. However, the evaluation of ischemic reduction after PCI was not the primary objective in the study and was based on sub-analysis; the number of patients evaluated was small and the patients had relatively mild ischemia with a pre-treatment ischemic total perfusion deficit being approximately 8%. In addition, because the study subjects were patients with stable effort angina, the data obtained from the nuclear sub-study cannot be applied to patients with history of MI and more severe cases, who should be cared for in usual clinical practice. Furthermore, there are no reports indicating such data in Japanese patients. We, therefore, have conducted this retrospective prognostic study in Japanese patients with CAD to evaluate quantitatively myocardial ischemia using SPECT before and after revascularization and to determine a relationship between the ischemic reduction and the incidence of cardiovascular events after the revascularization.

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

We retrospectively investigated 513 patients with CAD who underwent rest ^{201}Tl and stress ^{99m}Tc-tetrofosmin myocardial perfusion SPECT [6,9–13] at Nihon University Itabashi Hospital between October 2004 and March 2011 and who had a significant stenosis with 75% or greater narrowing of the coronary arterial diameter detected by coronary angiography (CAG) performed after confirmation of at least 5% ischemia by the SPECT. The patients underwent treatment including revascularization and medication, and thereafter were re-evaluated with the SPECT during a chronic phase and followed up to confirm prognosis for at least 1 year. The interval between the first SPECT and the CAG was 1.7 ± 3.4 months, that between the CAG and revascularization was 1.1 ± 4.5 months and that between the revascularization and the second SPECT was 10.3 ± 8.5 months. The second SPECT was performed at 14.1 ± 11.3 months after the first SPECT (Fig. 1). We excluded patients aged ≤20 years, those with hypertrophic or dilated cardiomyopathy, those with serious valvular heart disease, those with heart failure with class III or higher New York Heart Association (NYHA) functional classification, and those with less than 5% ischemia detected by the first SPECT.

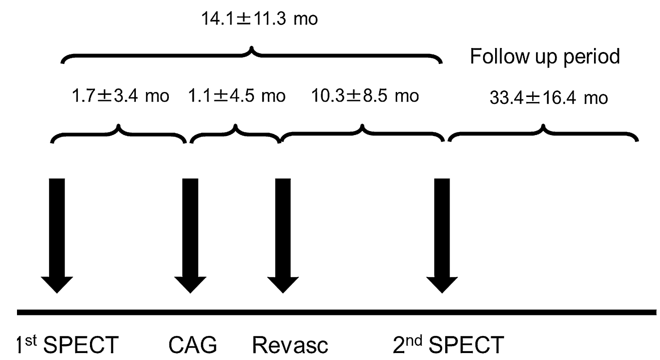

Fig. 1. Timing of nuclear cardiology, coronary angiography and revascularization. SPECT, single photon emission computed tomography; CAG, coronary angiography; Revasc, revascularization; mo, month.

Follow-up examinations were based on medical records for patients who periodically attended the hospital and responses to a posted questionnaire for patients who did not. The follow-up was successful for 483 patients (94%), but failed for the remaining 30 patients. Data from all 483 patients were finally included in the analysis.

Electrocardiogram-gated dual-isotope myocardial perfusion SPECT

The procedure of rest ^{201}Tl and stress ^{99m}Tc-tetrofosmin electrocardiogram (ECG)-gated myocardial perfusion SPECT was performed according to a protocol previously reported [6,9–13]. All patients received an intravenous (i.v.) injection of ^{201}Tl (111 MBq) and a 16-frame gated SPECT imaging 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 23% of the patients or by adenosine triphosphate in 77%. Sixteen-frame gated SPECT image acquisition was initiated 30 min after the exercise or 30–60 min after the adenosine triphosphate stress. The acquisition was performed in a supine position and subsequently in a prone position. 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 the stress.

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).

SPECT images were reconstructed from the data with a data processor (Philips North America, JETStream Workspace 3.0, Andover, MA, USA) combined with a Butterworth filter of ^{201}Tl (order 5; cut-off frequency 0.42 cycles/cm), that of ^{99m}Tc (order 5; cut-off frequency 0.44 cycles/cm) and a ramp filter.

SPECT image interpretation

The SPECT images were divided into 20 segments [14] on three short-axes (distal, mid, basal) and one on 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. The respective summed scores were converted into percent of the total myocardium (visual % myocardium). Visual % myocardium was derived from a summed score divided by the maximum potential score (4 × 20) and multiplied by 100.