Myocardial Perfusion Magnetic Resonance Imaging for Diagnosing Coronary Arterial Stenosis

Evaluation by Signal-intensity Time Curves

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SUMMARY

It has been reported that myocardial perfusion MRI is a useful method for evaluating the severity of myocardial ischemia. We evaluated whether the severity of coronary arterial stenosis could be assessed by the signal-intensity time curve (SITC) obtained by myocardial perfusion MRI.

The subjects consisted of 10 patients who showed no abnormalities on coronary angiographies (CAG) (A group), 12 with single-vessel disease of 75-90% stenosis on CAG (B group), and 15 with single-vessel disease of 90% or more stenosis (C group).

After infusion of dipyridamole for 4 minutes, gadolinium-diethylenetriamine pentaacetic acid was administered intravenously, followed by serial acquisition of T1-weighted left ventricular short-axis MR images. These images were evaluated after dividing them into the following 3 myocardial segments: anterior wall, lateral wall, and inferior wall. Mean values of the slope of SITC (1.4 ± 0.2 vs 1.1 ± 0.2, P < 0.01), and increases to the peak corrected SI (ΔSI) (47.5 ± 1.9 % vs 33.7 ± 2.4%, P < 0.01) in normal myocardial segments were significantly greater than in ischemic segments in the C group, while there was no significant distinction between normal and ischemic segments in the B group. The mean values of time to the peak SI were not significantly different between normal and ischemic regions in the B and C groups.

The results suggest that myocardial segments exhibiting 30% decreases in both the slope and ΔSI of SITC can be diagnosed as having 90% or more severe coronary stenosis. The present study shows that visual and SITC evaluations of myocardial perfusion MR images may be useful for clinically evaluating the severity of coronary stenosis. (Jpn Heart J 2003; 44: 323-334)

Key words: Perfusion MRI, Signal-intensity time curve, Myocardial ischemia, Coronary artery

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Received for publication July 19, 2002.

Revised and accepted October 21, 2002.
CORONARY angiography (CAG) is one of the most useful methods for diagnosing ischemic heart disease; its main drawback is its invasive nature. Myocardial scintigraphy offers patients a non-invasive diagnosis, but with higher medical expenses and radiation exposure. Myocardial perfusion magnetic resonance imaging (MRI) is a non-invasive method without the problem of radiation exposure. In addition, the spatial resolution of myocardial perfusion MRI is higher than that of myocardial scintigraphy. Developments in myocardial perfusion MRI have been accumulating rapidly; it has been reported to be more useful than myocardial scintigraphy (201-thallium single photon emission tomography) for detecting ischemic heart disease.1)

There are two methods for evaluating the severity of myocardial ischemia by myocardial perfusion MRI: 1) visual evaluation of the first pass kinetics of contrast media after intravenous bolus administration and 2) quantitative evaluation of serial changes in signal intensity (signal-intensity time curve; SITC) after the administration of contrast media. It has been reported that changes in signal intensity (SI) are smaller in ischemic myocardial regions compared to those in normally perfused regions,2) as SITCs may reflect myocardial blood flow (MBF). However, there have been few studies to evaluate the severity of coronary arterial stenosis using SITCs. In the present study, we investigated whether the severity of coronary artery stenosis can be evaluated by quantitative assessment of SITCs.

METHODS

Subjects: The subjects were 27 patients (17 men and 10 women, mean age: 68.7 ± 5.6 years) diagnosed with single vessel disease based on a suspicion of coronary artery disease, all of whom showed 75% or more stenosis on CAGs. Left ventriculography revealed that these 27 patients had normal cardiac function. The control group (A group) consisted of 10 patients who underwent CAG for evaluation of chest pain (7 men and 3 women, mean age: 68.7 ± 6.0 years) and who showed no coronary stenosis > 25% on CAGs. Patients with a past history of atrial fibrillation, unstable angina, or old myocardial infarction were excluded. Patients with coronary artery disease were classified into the following 2 groups based on the severity of their stenosis: a “B” group consisting of 12 patients with 75-90% stenosis and a “C” group consisting of 15 patients with 90% or more stenosis. Table I shows the clinical characteristics of the patients in the three groups. The study protocol was approved by our scientific ethics committee and conformed to the Declaration of Helsinki.

Coronary angiography (CAG): The angiographies were performed with a CAG system (Shimadzu Corp., 1 Tokyo) by inserting a 5 French Judkins catheter via the right femoral artery. The results were visually evaluated by 3 cardiologists.
Based on the severity of stenosis in the proximal region of the main coronary artery, the presence of 75% or more stenosis was defined as a significant stenosis, while the presence of less than 25% stenosis was defined as normal. Left ventriculography was performed in the 30-degree right anterior oblique projection, and the left ventricular (LV) ejection fraction was calculated by the area-length method.

MRI protocol: Within 1 week after CAG, myocardial perfusion MRI was performed with a 1.0 Tesla MRI apparatus (Signa, General Electric Medical Systems, Milwaukee, USA). Using a phased array coil, LV short-axis dynamic MR images (T1-weighted images) were acquired at the midventricular level (slice width: 10 mm). The pulse sequence was acquired by ECG gated fast spoiled gradient-recalled acquisition in the steady state (fast-SPGR) (repetition time: 6.7-6.8 ms, echo time: 2.5-2.6 ms, flip angle: 75°, field of view: 48 × 48 cm, matrix: 256 × 128). Subsequently, dipyridamole (0.56 mg/kg) was intravenously administered by drip infusion over 4 minutes via an 18-gauge needle in the right forearm vein. Two minutes after dipyridamole administration, 0.1 mmol/kg of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA, Magnevist Schering AG, Berlin, Germany) was rapidly administered intravenously, followed by 20 mL of saline solution. MR images were continuously acquired for 1 minute with the patient holding his or her breath as long as possible.

Perfusion MRI analysis: Acquired LV short-axis MR images were divided into the following 3 myocardial segments based on the distribution of major coronary arteries: anterior wall, lateral wall, and inferior wall (Figure 1). The presence or absence of myocardial ischemia in the respective segments was visually evaluated by 2 cardiologists and 1 radiologist, none of whom knew the results of the patient CAGs.
In order to compare the accuracy of myocardial perfusion MRI for diagnosing coronary arterial lesions with the results of CAG, the sensitivity and specificity were calculated separately in the left anterior descending artery (LAD), the left circumflex artery (LCX), and the right coronary artery (RCA).

Regions of interest (ROI) were manually established in the center of the myocardium to avoid pixels of the ventricular blood pool or epicardial fat (Figure 1); SI was measured in the respective segments. In addition, ROIs with a uniform size and configuration in each MR image were established to avoid the influence of respiratory motion. Corrected SI(t) was defined as follows: Corrected SI(t) = \[(SI(t) - SI(0)) / SI(0)\] × 100 (%) where SI(t) is the signal intensity at time t and SI(0) is the signal intensity before the contrast medium has reached the site (Figure 2).

The onset of the increase in the corrected signal intensity was visually assessed and considered the zero time point (T-0) as reported by Matheijssen, et al. Analysis of each subject’s SITC revealed peak corrected SI (ΔSI), time to the peak (t-peak), and slope of SITC (the ratio of ΔSI to t-peak). Comparisons of the results for normal and ischemic myocardial regions were used to determine the usefulness of SITCs of perfusion MRI in diagnosing myocardial ischemia.

**Statistical analysis:** All values are expressed as the mean ± standard deviation
Statistical analysis was performed using Statview 5.0 (SAS Institute Inc., Cary, NC, USA), and comparisons between two groups were performed using the unpaired $t$-test, paired $t$-test, and Fischer's exact test. In all cases, $P$ values less than 0.05 were considered significant.

RESULTS

MRI after administration of dipyridamole: After administering dipyridamole, MRI was successfully performed in all 37 patients without discontinuation. The mean heart rate was significantly increased after the administration of dipyridamole ($68.0 \pm 5.9$ min before vs. $78.1 \pm 6.7$ min after, $P < 0.0001$). Four patients in the C group complained of chest pain after the administration of dipyridamole; intravenous drip infusion of aminophylline was required in 2 patients. However, severe complications such as hypotension, serious arrhythmias or myocardial infarction were not observed in any patients. Insufficient breath holding in 1 patient in the B group and 2 patients in the C group produced severe artifacts during the acquisition of MR images; these 3 patients were excluded from this study. Eventually, myocardial perfusion MR images from 11 patients in the B group (33 myocardial segments) and 13 patients in the C group (39 myocardial segments) were visually evaluated, and SITCs for a total of 102 myocardial segments were successfully prepared in 34 subjects in the A, B, and C groups.
Visual evaluation of LV short-axis MR images: Figure 3 shows a representative MR image in a 66-year-old man with 99% stenosis in segments #11, #12, and #13 (AHA classification) of the left circumflex artery. Eight seconds after the injection of Gd-DTPA, the contrast medium flowed into the right ventricle and then reached the left ventricle. The contrast medium distributed throughout the entire myocardia 12 seconds after the injection, resulting in increased SI in the myocardium. Since increases in SI were delayed in the lateral wall, a low SI was initially observed in the lateral wall.

When the accuracy of myocardial perfusion MRI for diagnosing coronary arterial lesions was evaluated based on the results of CAG in the B group, the sensitivity was 55% (50% for LAD lesions, 67% for LCX lesions, and 50% for RCA lesions) and the specificity was 77% (86% for LAD lesions, 75% for LCX lesions, and 71% for RCA lesions). In the C group, the sensitivity was 77% (75% for LAD lesions, 80% for LCX lesions, and 75% for RCA lesions) and the specificity was 81% (100% for LAD lesions, 75% for LCX lesions, and 67% for RCA lesions).
The diagnostic accuracy of myocardial perfusion MRI increased with the severity of the coronary arterial lesions.

**Evaluation of SITC analysis:** The mean $\Delta SI$ of the anterior, lateral, and inferior walls in the regions normalized by those of the normal coronary artery was 49.4%, 47.9%, and 47.5% in the A group; 48.9%, 47.1%, and 47.4% in the B group; and 49.0%, 46.4%, and 47.2% in the C group, respectively. The mean $\Delta SI$ was slightly higher on the anterior wall than on the other walls, but there was no statistically significant difference. Figure 4 shows the SITC of the same patient as in Figure 3. In this patient, the slopes of the SITC and $\Delta SI$ were 1.7 and 52.1% in the anterior wall, 1.7 and 50.2% in the inferior wall, and 1.2 and 35.4% in the lateral wall, respectively. In addition, the slopes of the SITC and $\Delta SI$ in the lateral wall were lower than those in the normal myocardial region by 29.4% and 30.9%, respectively.

Table II shows the comparison of SITCs among the A, B, and C groups. The A group was used to obtain mean values of the respective parameters (slope, $\Delta SI$, and $t$-peak) in 3 myocardial segments (anterior wall, lateral wall, and inferior wall) to be used as norms for SITC in perfused myocardial regions without coronary arterial lesions (N-regions). In the B and C groups, the mean values of the respective parameters in 2 normally perfused myocardial segments without coronary arterial stenosis were also used as SITC parameters of N-regions.

In the B group, the mean value of the slope in the ischemic myocardial segments with coronary arterial lesions (I-regions) was lower by 6.1% than that in N-
regions of the B group, although this decrease was not significant, even when compared to N-regions of the A and C groups. The mean value of $\Delta SI$ in I-regions of the B group tended to be 5.9% lower than that in N-regions of the B group, although this decrease did not reach the level of statistical significance. However, the mean value of $\Delta SI$ in I-regions of the B group was significantly lower than that in N-regions of the A group ($P < 0.05$).

In the C group, the mean value of the slope in I-regions was lower by 28.4% than that in its N-regions, and this decrease was also significant in relation to the slopes of N-regions in the other 2 groups ($P < 0.01$). The mean value of $\Delta SI$ in I-regions of the C group was lower by 28.7% than that of N-regions, and this decrease was also significant in relation to $\Delta SI$ in N-regions of the other 2 groups ($P < 0.01$). However, there were no significant differences in the mean values of t-peak between I-and N-regions in the B and C groups.

**DISCUSSION**

Since myocardial perfusion MRI facilitates the non-invasive diagnosis of coronary artery disease, many studies have reported its usefulness. The sensitivity and specificity of MRI for visually diagnosing coronary artery disease based on CAG findings have been reported to be 70-83% and 83-100%, respectively.\(^1\text{-}^7\)

SI is generally higher in the anterior wall than in the interior wall. This is because SI in each cardiac region is greatly influenced by the distance from the superficial coil. In the present study, the effects of the sensitivity of the coil were corrected in each cardiac region using corrected SI. There were no significant differences in the $\Delta SI$ of the anterior, lateral, and inferior walls in the regions normalized by the normal coronary artery among the groups. Therefore, the differences in $\Delta SI$ between the ischemic and normal regions were considered to reflect differences in the coronary blood flow rate.
In the present study, quantitative evaluation of serial changes in signal intensity, namely the slope of SITC and ∆SI, were useful indicators for evaluating the severity of coronary arterial stenosis. The results also suggest that a decrease of 30% in both the slope and ∆SI of SITC is a good indicator for 90% or more severe coronary stenosis in the myocardial segments exhibiting such features.

There have been many studies on the diagnosis of ischemic heart disease by myocardial perfusion MRI using a 1.5 Tesla MRI apparatus. The diagnostic accuracy of myocardial perfusion MRI may vary depending on the strength of the magnetic field, pulse sequences, and time resolution of the MRI apparatus, the number of acquired MR images, and the severity of coronary arterial lesions. However, it has been reported that suitable diagnostic accuracy was obtained using a 0.5-1.0 Tesla MRI apparatus, as Keijer, et al reported that the accuracy of a 1.0 Tesla MRI apparatus for diagnosing ischemic heart disease did not significantly differ from that of a 1.5 Tesla MRI apparatus.

A number of studies have investigated the usefulness of perfusion MRI for the diagnosis of ischemic heart disease based on visual evaluation of the first pass kinetics of the contrast media. Panting, et al used LV short-axis images acquired by echo planar imaging (EPI) (0.5 Tesla), and reported that the sensitivity and specificity of perfusion MRI for diagnosing 50% or more coronary arterial stenosis were 77% and 83%, respectively. Hartnell, et al evaluated the accuracy of perfusion MRI for diagnosing 70% or more coronary arterial stenosis using turbo fast low-angle shot (1.0 Tesla), and reported that the sensitivity and specificity were 83% and 100%, respectively. The values from these two studies are comparable to those of the present study in relation to the severity of the stenosis.

Other studies have evaluated SITC as a tool for detecting and diagnosing ischemic heart disease. Manning, et al quantitatively evaluated SITCs in 17 patients with 80% or more coronary arterial stenosis, and reported that the mean values of the slope and peak intensity of SITC in ischemic myocardial regions were respectively lower by 32% and 21% than those in normal myocardial regions. Furthermore, Panting, et al quantitatively analyzed the slope and peak intensity of SITC, and reported that the sensitivity and specificity of myocardial perfusion MRI for diagnosing coronary arterial lesions based on the slope of SITC were 79% and 83%, respectively. They also noted that the sensitivity and specificity based on the peak intensity of SITC were 72% and 83%, respectively. Thus, it has been reported that increases in the slope and signal intensity of SITC are useful indices for evaluating the degree of myocardial perfusion.

Although the presence or absence of myocardial ischemia may be diagnosed by visually and quantitatively evaluating the first pass kinetics of contrast media using myocardial perfusion MRI, few studies have evaluated the first pass kinetics of contrast media according to the severity of coronary arterial stenosis. Clin-
ical evaluation of the severity of coronary arterial stenosis is important to determine the therapeutic strategy for ischemic heart disease. Since coronary arterial blood flow decreases with the severity of coronary arterial lesions, SITCs are expected to vary with the severity of coronary arterial lesions. The present study tested whether the severity of coronary arterial lesions can be evaluated accurately by quantitative assessment of SITCs.

Using positron emission tomography (PET), Uren, et al. measured myocardial blood flow (MBF) in patients with a single vessel coronary arterial lesion. After intravenous administration of the vasodilator adenosine or dipyridamole, they found that myocardial blood flow progressively decreases when the degree of stenosis is about 40% or more and does not differ significantly from basal flow when stenosis is 80% or greater. In addition, Carli, et al. reported that favorable MBF was maintained at rest before the development of 70% or more stenosis. Thus, in order to diagnose ischemic heart disease using SITCs, myocardial stress testing is suggested to be essential.

In the present study, when 3 parameters of SITC (slope, \(\Delta SI\), and t-peak) obtained after dipyridamole administration were compared between normal and ischemic regions, the mean values of the slope and \(\Delta SI\) were lower by approximately 6% in ischemic regions located in the perfusion area of the coronary artery with 75-90% stenosis. In addition, the mean values of the slope and \(\Delta SI\) were lower by approximately 30% in ischemic regions located in the perfusion area of the coronary artery with 90% or more stenosis. These findings suggest that the severity of coronary arterial stenosis can be diagnosed by semiquantitative evaluation of SICTs; the values of the slope and \(\Delta SI\) decrease dramatically with the increased severity of coronary arterial lesions.

Previous studies have reported that t-peak of SICT is not useful for evaluating the severity of coronary arterial stenosis. In the present study, the mean values of t-peak did not differ significantly between normal and ischemic regions, probably because the time resolution was limited. Since MR images were acquired at 3-4 second intervals, changes in SI under 4 seconds or shorter were not reflected in the results. It is possible that a higher time resolution is required to evaluate the kinetics of myocardial perfusion based on t-peak. Further advances in MRI hardware and software are expected to address this need.

**Limitations of the study:** Since a general purpose MRI apparatus was used in the present study, multisectional short-axis MR images were not acquired. In addition, this study evaluated a single LV short-axial section at the midventricular level; the entire heart was not evaluated. Since some ischemic changes may not be detected by evaluating a single LV short-axial section, multisectional images are required to diagnose coronary arterial lesions, especially those in distal sections.
In patients with multivessel coronary artery disease, it is difficult to compare SITCs between normal and ischemic regions because blood flow decreases in the 3 major coronary arteries. However, the presence of myocardial ischemia may be diagnosed by comparing SITCs between patients with multivessel coronary artery disease and normal subjects. Further research on SITC quantitative analysis is needed to improve the diagnostic capacity of such comparisons.

Thus, the methods and results of the present study could not be simply applied to all cases of coronary heart disease. However, the evaluation of SITCs may facilitate the diagnosis of ischemic heart disease and the severity of coronary arterial lesions. Clinical application of such quantitative methods applied to myocardial perfusion MRI can be expected in the near future.

**Conclusions:** The quantitative evaluation of the slope and ∆SI obtained by the SITC may facilitate the evaluation of the severity of coronary arterial lesions. In the near future, the diagnostic accuracy of myocardial perfusion MRI may be increased by supplementing the results of visual evaluation with SITC information and analysis.

**REFERENCES**