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# The Usefulness of Stress Perfusion MR using Steady State Free Precession Sequence for Depiction of Significant Coronary Artery Stenosis

Se-Yeong Chung, M.D., Sang Il Choi, M.D.[2], Dong Hoon Kim, M.D.[3], Hyuk-Jae Chang, M.D.[4], Dong Ju Choi, M.D.[4], Cheong Lim, M.D.[5], Whal Lee, M.D., Jae-Hyung Park, M.D.

**Purpose:** To evaluate the technical performance of stress myocardial perfusion magnetic resonance (MR) imaging using saturation-recovery steady-state free precession (SR- SSFP) and to assess the diagnostic accuracy of this examination for depiction of significant coronary artery stenosis.

**Materials and Methods:** 167 patients underwent stress myocardial perfusion MR imaging at rest and adenosine-induced stress by using a 1.5-T cardiac MR imaging unit. The first-pass MR perfusion was performed using SR-SSFP sequence. Coronary angiography was performed in 113 patients. Image analysis was performed to compare the diagnostic accuracy of MR imaging with that of coronary angiography.

**Results:** During the MR examination, minor side effects of adenosine-induced stress occurred, most commonly chest discomfort (29%), followed by dyspnea (4%), and facial flushing (0.8%). The overall sensitivity of MR imaging for depicting at least one coronary artery with significant stenosis was 91%. The sensitivities of MR imaging for depiction of stenoses were as follows: 80% for single-vessel stenosis, 81% for double-vessel stenosis, and 100% for triple-vessel stenosis.. The specificity of MR imaging for identification of patients with significant coronary artery stenosis was 78%.

**Conclusion:** Stress myocardial magnetic resonance (MR) perfusion imaging using SR-SSFP sequence is safe and useful for the detection of significant coronary artery disease.

**Index words :** Myocardium
Magnetic resonance (MR)
Coronary vessels, diseases

[1]Department of Radiology and Institute of Radiation Medicine, Seoul National University College of Medicine, Clinical Research Institute, Seoul National University Hospital, Seoul, Korea
[2]Department of Radiology, Seoul National University Bundang Hospital, Korea
[3]Department of Radiology, Chosun University, Korea
[4]Department of Internal medicine, Division of Cardiology, Seoul National University Bundang Hospital, Korea
[5]Department of Thoracic Surgery, Seoul National University Bundang Hospital, Korea
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Address reprint requests to : Sang Il Choi, M.D., Department of Radiology, Seoul National University Bundang Hospital, 300 Gumi-dong, Bundang-gu, Seongnam-si, Gyeonggi-do 463-707, Korea
Tel. 82-31-787-7609 Fax. 82-31-787-4011 E-mail: drsic@radiol.snu.ac.kr

Coronary artery disease (CAD) remains the leading cause of death worldwide (1). Catheter-based radiographic angiography is the gold standard in diagnosing coronary artery disease. However, this technique has many disadvantages, including associated morbidity, radiation exposure, need for a potentially nephrotoxic contrast agent, and high costs. Such disadvantages favor a noninvasive alternative. Single photon emission computed tomography (SPECT) is widely used for myocardial perfusion in clinical practice, with sensitivities as high as 83% to 95% and specificities ranging from 53% to 95% (2 - 4).

However, the major drawbacks in the use of SPECT are low spatial resolution and the occurrence of attenuation artifacts, which can be found at the anterior wall in obese women with large breasts and at the inferior wall in men due to respiratory excursion (5). Although myocardial perfusion can be quantitatively assessed with PET, the technique is limited by its reduced availability.

Magnetic resonance imaging (MRI) is a developing alternative to SPECT and can potentially produce perfusion images with higher spatial resolution without attenuation artifacts and ionizing radiation. Recently, stress perfusion MRI using saturation-recovery steady-state free precession sequence (SR-SSFP) has been proven to provide higher signal-to-noise and contrast-to-noise ratios than fast gradient techniques (6, 7). Therefore, the purpose of this study is to evaluate the technical performance and assess the diagnostic accuracy of SENSE-accelerated myocardial perfusion cardiac MR imaging for the depiction of significant coronary artery stenosis.

## Materials and Methods

### *Study Population*

This retrospective study included 167 patients, whose medical records were retrospectively reviewed, who underwent stress perfusion MRI between January 2004 and April 2005. Among them, 113 patients underwent both coronary angiography and stress perfusion MRI. We recruited patients who had undergone both stress perfusion MRI and coronary angiography within the past 30 days. A total of 113 patients were included in this study. There were 71 men and 42 women ranging in age from 39 - 82 years old (mean age was 62.1 years ± 9.6 [SD] ).

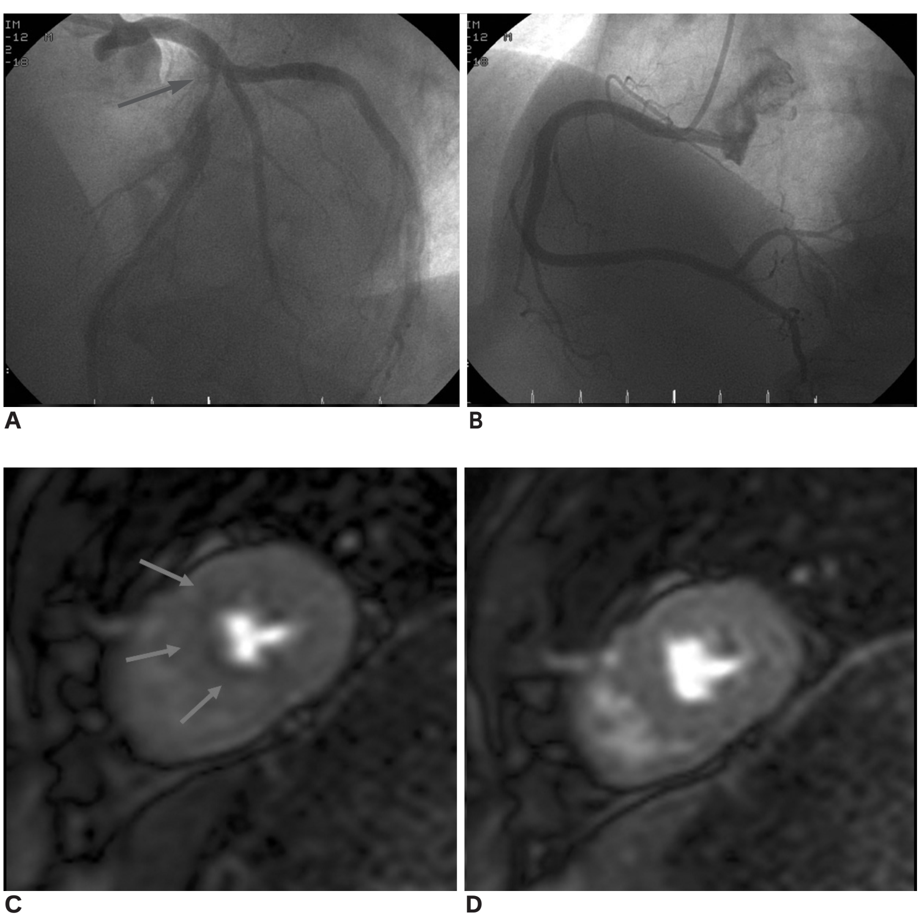


**Fig. 1.** 63-year-old male with single-vessel disease. (Fig. 1**A**) Coronary angiography shows 90% segmental stenosis at left anterior descending coronary artery from os to proximal portion (arrow). (Fig. 1**C, D**) MR perfusion imaging reveals reversible subendocardial perfusion defect at left anterior descending coronary artery territory (arrows).

Patients with a history of recent myocardial infarction (less than 2 weeks earlier), prior coronary artery bypass graft surgery, or percutaneous coronary artery stenting were excluded from this study.

### MR Imaging

Patients underwent perfusion MR imaging at rest and under stress by using a 1.5-T Intera CV release 10 cardiac MR imaging unit (Philips Medical Systems, Best, Netherlands) equipped with high-performance gradients for cardiac MR imaging (maximum slew rate = 150 T/m/sec, gradient strength = 40 mT/m ) and a five-element phased-array cardiac coil. Electrocardiographic gating and triggering were performed using a vectorcardiographic method (8). To ensure minimal basal blood flow and a maximal vasodilatory response to adenosine, patients were instructed to refrain from smoking, tea, or coffee, as well as ß-blockers and antianginal medication, for 24 hours before the examination.

Fast survey images were acquired to determine the true short axis of the left ventricle. Then, a low-spatial-resolution reference image was acquired to serve as the three-dimensional fast field-echo coil sensitivity map (7° flip angle, 530×530-mm field of view, 32×26 matrix, two stacks of 50 coronal sections) that is acquired with use of SENSE.

At-rest perfusion was assessed by using the segmented k-space gradient-echo saturation-recovery T1-weighted turbo field-echo pulse sequence. The three MR image sections were distributed to cover the heart between the outflow tract and the apex by adjusting the gap between the sections. The first section covered the basal segment, the second section covered the middle segment, and the last third section covered the apical segment. A dynamic series of images was acquired continuously for 40 seconds, with 10 baseline images obtained during an initial expiratory breath hold. This was followed by two respiratory cycles and an additional breath hold that typically lasted 20 seconds and was timed to correspond to the interval of the first pass of the contrast material bolus. During the inspiratory phase of the second breath, a bolus of gadodiamide (Omniscan; GE health-

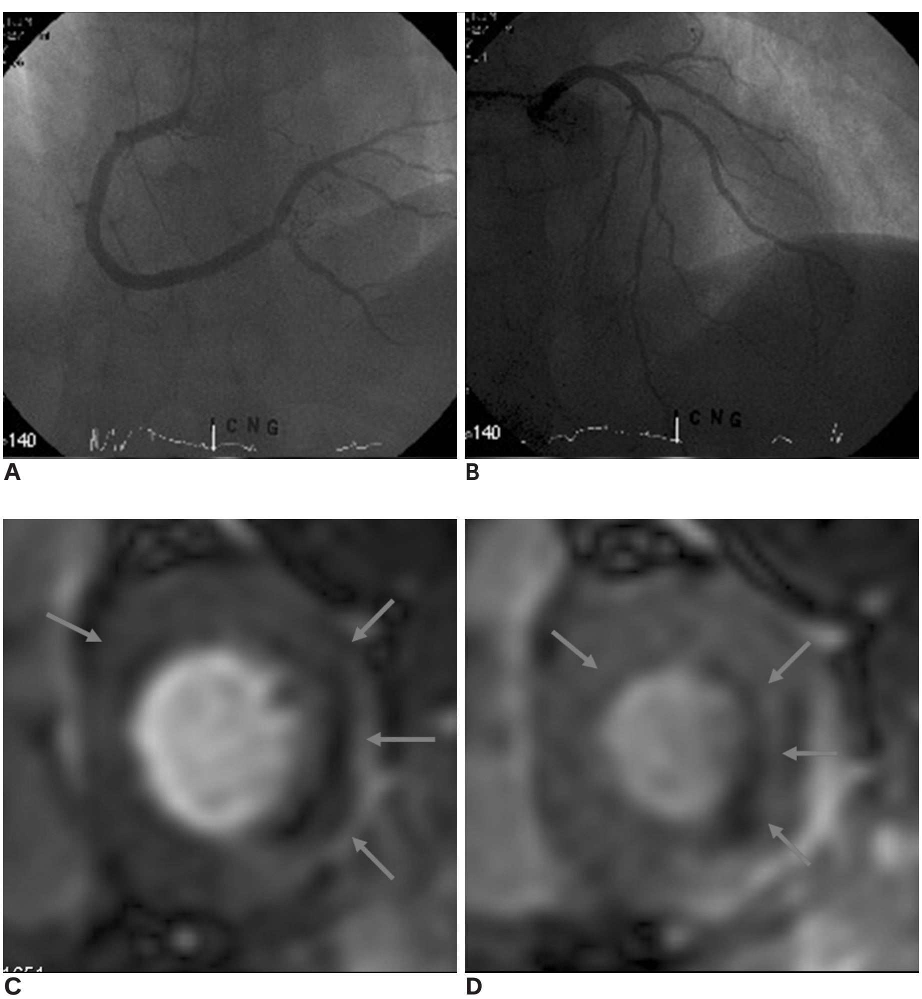

**Fig. 2.** 47-year-old male patient with two- vessel disease. (Fig. 2**A**) Coronary angiography shows no significant steno-occlusive lesion in right coronary artery. (Fig. 2**B**) Multifocal severe stenosis at left anterior descending and left circumflex coronary artery is present. Perfusion MRI at stress (Fig. 2**C**) and rest (Fig. 2**D**) reveals partially reversible perfusion defect at anterior, anterolateral, and inferolateral wall, suggesting myocardial ischemia of left anterior descending and left circumflex coronary artery territory (arrows).

care, U.S.A.) at a dosage of 0.1 mmol per kilogram of body weight was injected at a rate of 4 mL/sec into an antecubital vein using a power injector (Spectris; Medrad, Indianola, Pa). This procedure was followed by a 20 mL-saline flush. After 30 minutes, to allow adequate clearance of the first bolus of the contrast agent, adenosine was infused at a dose of 0.14 mg/kg body weight/min for up to 6 minutes. During adenosine infusion, electrocardiographic activity was monitored continuously, and blood pressure and heart rate measurements were obtained at one- minute intervals. A second perfusion image acquisition was commenced in the same plane after 4 minutes of adenosine infusion with the same acquisition sequence that was used for the at-rest images.

Between the two perfusion image acquisitions, a multisection multiple-phase data set of 10 - 12 short-axis cine images sections to cover the entire left ventricle was acquired using a balanced steady-state free precession technique (2744/1372 msec: TR/TE, 50 °flip angle, 256×256 matrix, 8 - 10 mm section thickness, 8 - 10 mm intersection gap).

### *Image Analysis of Stress perfusion MRI*

Two experienced investigators [one observer with 11 years of experience in cardiac MR imaging (S.I.C.), the other observer with 3 years of experience in cardiac MR imaging (S.Y.C.)] qualitatively evaluated MR images by consensus without knowing clinical information or results from other studies. Rest and stress perfusion MR images were displayed side by side on a workstation. Perfusion MR images were evaluated by manually paging the images. Semi quantitative analysis was not performed in this study. Images of the left ventricular myocardium were divided into 16 segments that were defined to correspond to segments 1 - 16 of the 17-segment model recommended by the American Heart Association (9). We compared the perfusion MR images at rest and stress to differentiate artifacts from low enhancement caused by coronary artery stenosis. Perfusion defect was defined to be present on stress MR images when persistent low enhancement was observed

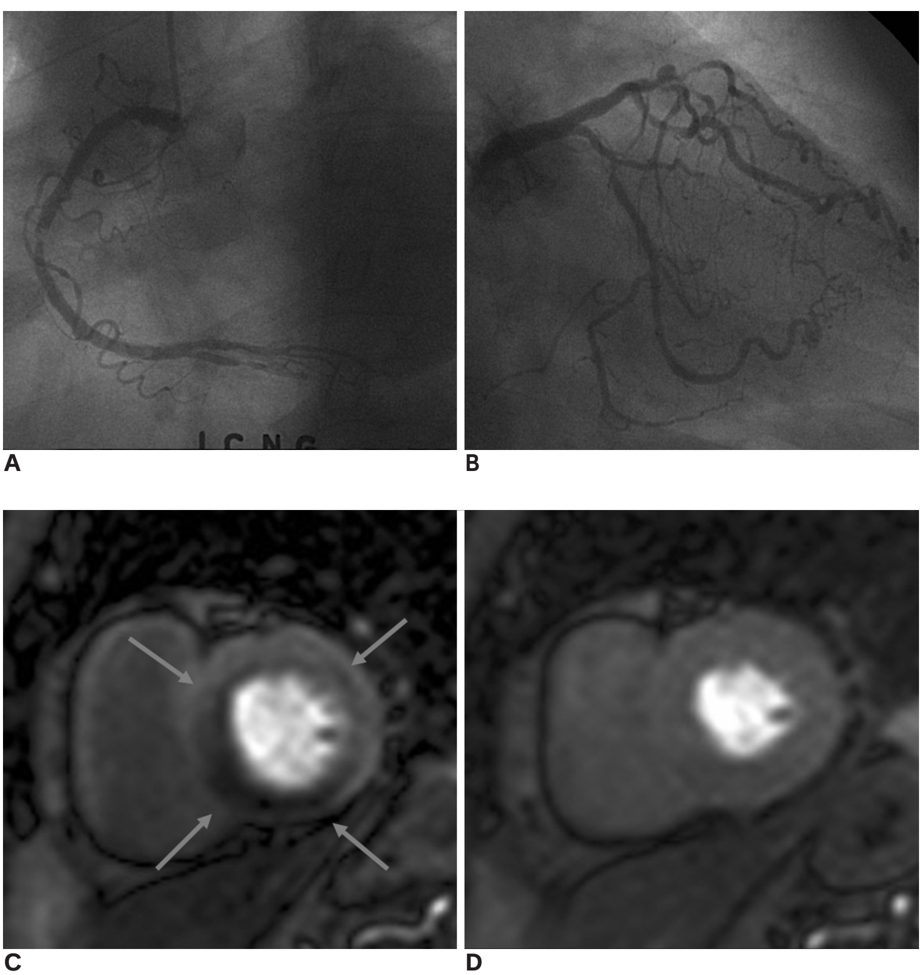


**Fig. 3.** 84-year-old woman with three-vessel disease. (Fig. 3**A**, Fig. 3**B**) Coronary angiography shows focal tight stenosis at mid- right coronary artery and diffuse severe stenosis at left anterior descending and left circumflex coronary artery. Perfusion MRI at stress (Fig. 3**C**) and at rest (Fig. 3**D**) reveals a ring of reversible subendocardial perfusion defect at whole vascular territory (arrows).

on at least three consecutive images from the first pass of MR contrast agent through the myocardium. Stenotic coronary artery disease was considered present if a myocardial perfusion defect was present during stress that was not observed at rest. A dark band or rim along the subendocardial border of left ventricle was considered an artifact due to Gibbs ringing if it did not remain after passage of the bolus (10). For comparison with invasive coronary angiography, perfusion defect segments were related to the corresponding presumed coronary artery territories.

#### *Coronary Angiography and Image Interpretation*

All patients underwent conventional coronary angiography using 5-F high-flow Judkins catheters (Cordis, Miami, FL, U.S.A.) and images were acquired in multiple projections. Coronary artery stenosis was imaged in the center of the field from multiple projections; overlap of side branches and foreshortening of relevant coronary arteries were avoided as much as possible. After selecting the projection that showed maximal severity, the luminal diameter of the stenotic artery, along with adjacent reference segments, was measured on the end-diastolic frame. The severity of the stenosis was expressed as a percentage reduction of the internal diameter in relation to the estimated diameter interpolated from the diameters at the proximal and distal boundaries of the stenosis.

Retrospective analysis of the coronary angiograms was performed using a validated quantitative coronary angiographic system (Philips H5000, Philips Medical Systems, Andover, MA, USA, or Allula DCI program, Philips Medical System, Best, The Netherlands) by an experienced cardiologist (H.J.J., 7 years of experience), who was uninformed as to patient history and the results of the MR examination.

Presence of ≥70% narrowing of the left anterior descending artery, right coronary artery, and left circumflex artery, or their major branches was considered significant.

#### *Statistical Analysis*

Continuous variables were expressed as the mean value ±1 standard deviation. Non-continuous categorical variables were expressed as sums and percentages. Sensitivity, specificity, diagnostic accuracy, and positive and negative predictive values were calculated according to standard definitions. Statistical significance was assumed with a *P* value of less than .05. All data was analyzed with the use of commercially available software (MedCalc, version 8.0.0.1, MedCalc Software, Mariakerke, Belgium).

## Results

#### *Safety and Feasibility of stress perfusion cardiac MRI*

Stress perfusion cardiac MR imaging was performed successfully in all 113 patients without contraindications to cardiac MR imaging. During stress testing, heart rate increased from 74±12.2 beats per minute to 83.5±13.6 beats per minute, systolic blood pressure decreased from 147±22.8 mmHg to 137.6±27.6 mmHg, diastolic blood pressure decreased from 75.5±11.8 mmHg to 70.5±11.9 mmHg. Chest discomfort occurred in 33 patients (24.8 %), dyspnea occurred in 5 patients (4%), and facial flushing occurred in one patient (0.9%). No patient experienced life-threatening or serious adverse reactions during pharmacological stress. Adequate image quality for diagnosis of stress perfusion MRI was obtained in all patients. None of the images had to be excluded because of susceptibility or ghosting artifacts. In three of the patients, thin subendocardial susceptibility artifacts were seen on the apical section during arrival of the contrast material bolus in the left ventricle, but these artifacts disappeared during myocardial enhancement. No stress cardiac MR imaging was terminated prematurely, and all stress perfusion MR imaging examinations were completed within 60 minutes.

#### *Overall Detection of CAD*

During invasive coronary angiography, 214 coronary arteries with significant stenoses were found in 90 patients (80%), while 23 patients (20%) had no significant stenoses. Fifteen patients had single-vessel disease, 26 had double-vessel disease, and 49 had triple-vessel disease. When compared with quantitative coronary angiography, the overall sensitivity of MR imaging for depicting at least one coronary artery with significant stenosis was 91% (82 of 90 patients). The sensitivities of MR imaging were 80% (12 of 15 patients) for depiction of single-vessel stenoses, 81% (21 of 26 patients) for double- vessel stenoses, and 100% (49 of 49 patients) for triple -vessel stenoses. The specificity of MR imaging for identification of patients with significant coronary artery stenosis was 78% (18 of 23 patients). The positive predictive value was 94.2% (82 of 87 patients), the negative predictive value was 69.2% (18 of 26 patients), and accuracy was 88.4% (100 of 113 patients).

## Discussion

Our results show that stress perfusion MRI using SR-SSFP sequence is safe and useful for the detection of significant coronary artery stenosis. Recently, Sakuma et al (11, 12) used saturation-recovery turbo FLASH sequence for detecting significant stenosis. They reported that in at least one coronary artery the sensitivity was 81.0%, specificity was 68.4%, positive predictive value was 73.9%, negative predictive value was 76.5%, and accuracy of stress perfusion MRI was 75.0%.

In our study, the overall sensitivity and positive predictive value of stress perfusion MRI in depicting significant coronary artery disease was substantially higher than in the previous study. This result may be due to the relatively large number of patients with three-vessel coronary artery disease in this study (43.3% or 49 of 113 patients). With recent advances in MR imaging techniques, including saturation-recovery steady-state free precession sequence, the diagnostic capability of MR myocardial perfusion imaging has been proven to provide high signal-to-noise ratios and contrast-to-noise ratios (6, 7). Hunold et al (7) suggested that SR-SSFP sequence was better than fast gradient techniques for providing a delineation between ischemic and normally perfused myocardium because of higher signal-to-noise ratios . Previous studies using MRI have demonstrated that alterations in myocardial perfusion can be assessed by using MR imaging (13 - 15) using gradient echo sequence. However, previous studies were not specifically designed to study the usefulness of SR-SSFP sequence for stress MR perfusion imaging and did not involve a large number of patients .

In our study, the overall sensitivity and positive predictive value of stress perfusion MRI in depicting significant coronary artery disease was substantially higher than those observed in previous studies. This result may be due to the relatively large number of patients with three-vessel coronary artery disease in this study (43.3% or 49 of 113 patients). The higher degree of spatial resolution of MR imaging using SR-SSFP enables better delineation of small subendocardial ischemia and may explain the improved diagnostic performance in the detection of perfusion abnormalities.

There are several limitations in our study. First, we only visually analyzed stress perfusion MRI and SPECT, and no quantitative assessment of stress perfusion MR imaging was performed. Quantitative assessment of stress MRI with correction for inhomogeneous coil sensitivity may further improve the sensitivity and specificity of stress perfusion MR imaging. Second, our results were retrospectively analyzed in a relatively limited number of subjects with a high prevalence of coronary artery disease. Further study with multi-center trials is required to determine the diagnostic performances of stress perfusion MRI using SR-SSFP sequence.

Third, we regarded coronary angiography as the reference standard in the diagnosis of ischemic heart disease. Coronary artery angiography can visualize the grade of epicardial coronary stenosis; however, it cannot assess the functional relevance of luminal obstruction or presence of collateralization with respect to end-organ perfusion. Therefore, further study is required to determine the relative diagnostic accuracy of stress perfusion MRI when compared to stress perfusion scintigraphy such as SPECT and PET.

In conclusion, stress myocardial magnetic resonance perfusion imaging using SR-SSFP sequence is safe and useful for the detection of coronary artery stenosis.

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# 관상동맥협착의 진단에 있어 항정상태 자유세차운동 기법을 이용한 부하 심근 관류 자기공명영상의 유용성[1]

[1]서울의대 진단방사선과학교실, [2]분당서울대학교병원 진단방사선과, [3]조선의대 진단방사선과학교실, [4]분당서울대학교병원 심장내과, [5]분당서울대학교병원 흉부외과

정세영 · 최상일[2] · 김동훈[3] · 장혁재[4] · 최동주[4] · 임 청[5] · 이 활 · 박재형

**목적:** 관상동맥 협착의 진단에서 항정상태 자유세차운동 기법을 이용한 부하 심근 관류 자기공명영상의 유용성을 알아보고자 하였다.
**대상과 방법:** 부하 및 휴식기 심근 관류 자기공명영상을 시행 받은 167명의 환자를 대상으로 하였으며, 항정상태 자유세차운동 기법을 이용하여 초기 심근관류 자기공명영상을 얻었다. 관상동맥 조영술은 113명에서 시행되었으며, 이를 표준검사로 하여 부하 심근 관류 자기공명영상의 진단적 정확도를 평가하였다.
**결과:** 아데노신 부하 심근 관류 자기공명영상을 시행하는 동안 흉부 불편감(29%), 경도의 호흡곤란(4%), 및 안면 홍조(0.8%)의 가벼운 부작용이 있었다. 적어도 한 개 이상의 의미 있는 관상동맥 협착을 가진 환자에서의 자기공명영상의 민감도는 91%이었다. 1, 2, 3 혈관의 의미 있는 관상동맥 협착의 진단에서 자기공명영상의 민감도는80%, 81%, 100%였다. 70% 이상 관상동맥 협착을 가진 환자에게서의 자기공명영상의 특이도는 78%이었다.
**결론:** 관상동맥협착의 진단에서 항정상태 자유세차운동기법을 이용한 부하 심근 관류 자기공명영상 기법은 안전하며 유용하다.