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Assessment of Coronary Flow Velocity Reserve Using Fast Velocity-Encoded Cine MRI for Noninvasive Detection of Restenosis After Coronary Stent Implantation

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ABSTRACT

Purpose: *Serial change of the coronary flow velocity reserve was evaluated with fast velocity-encoded cine magnetic resonance imaging (MRI) for noninvasive detection of restenosis after coronary stent implantation.* ***Method:*** *In total, 60 MRI flow studies were performed in 10 patients with coronary artery disease who underwent elective successful stent implantation to the lesion in the proximal left anterior descending artery. Flow velocities in the segment that was distal to the stent were measured before and after intravenous injection of dipyridamole. MRI measurements of coronary flow velocity reserve were repeated every 4 weeks for 6 months, and follow-up angiography was performed 6 months after the procedure. Results: In patients without restenosis (*n = 7*, % diameter stenosis: 27.8% ± 7.1) at follow-*

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*up angiography, the coronary flow velocity reserve remained normal during the 6-month follow-up time. The flow velocity reserve was 2.31 ± 0.30 at 1 month and 2.52 ± 0.25 at 6 months after stent implantation (*p *= NS). In contrast, the coronary flow velocity reserve showed a significant decrease after 4 months in patients with restenosis (*n *= 3, % diameter stenosis: 66.3% ± 8.1) at follow-up angiography. The flow velocity reserve was 2.26 ± 0.49 at 1 month and 1.52 ± 0.09 at 6 months after stent implantation (*p *< 0.05).* ***Conclusion:*** *Fast velocity-encoded cine MRI is a technique that shows promise in providing non-invasive detection of restenosis of coronary stent implantation.*

Key Words: *Coronary flow velocity reserve; MR imaging; Stent; Restenosis*

INTRODUCTION

The long-term benefit of coronary balloon angioplasty has been limited by the possibility of restenosis of the treated segment (1–4). Although placement of intracoronary stent has reduced the rate of restenosis, incidence of restenosis after stent implantation is not negligible (5–6). Early identification of patients who develop coronary arterial restenosis has important diagnostic and therapeutic implications. Restenosis of the coronary artery has been evaluated mostly with X-ray coronary angiography. However, this technique is invasive and is not suited for screening patients without clinical evidence of angina after coronary interventions. A noninvasive method that can detect restenosis would be highly useful in managing patients after balloon angioplasty and stent implantation. The functional significance of coronary arterial stenosis can be evaluated by measuring coronary flow reserve, that is the ratio of maximal hyperemic to the baseline coronary flow (7). Recently, several studies have demonstrated the feasibility of measuring coronary flow reserve in patients by using fast velocity-encoded cine MRI (8–9). The purposes of these studies were to investigate serial changes of the coronary flow velocity reserve using fast velocity-encoded cine MRI in patients after stent implantation and to determine whether this MRI method can provide a noninvasive detection of coronary arterial restenosis.

Methods

Ten consecutive patients (7 men and 3 women; ages 44 to 72 years, mean = 59) underwent successful stent implantation in the proximal left anterior descending (LAD) coronary artery were enrolled. This study was approved by the Institutional Ethics Committee and all patients gave informed consent. All subjects had a history of stable angina, and a single, significant coronary arterial stenosis in the proximal LAD artery documented in coronary angiography. The patients with myocardial infarction, coronary artery bypass grafting, or prior balloon angioplasty were excluded. Coronary angioplasty was performed from the femoral artery approach. After predilatation, the stents were deployed by inflating the stent delivery balloon at nominal pressure (Palmaz-Schatz stent: 8 cases, GFX stent: 1 case, Wiktor stent: 1 case), and adjunct high-pressure balloon dilatation was performed to achieve angiographic optimization. Procedural success (defined as successful stenting at the desired position with ≤30% residual stenosis on visual estimation) was obtained in all patients. All patients were asymptomatic for at least 6 months after coronary stent implantations. Selective coronary angiography was performed at 6 months (195 ± 32 days) in all patients in order to evaluate restenosis in the LAD artery.

The initial MRI measurements of the coronary flow velocity reserve were obtained at one month after stent implantation and were repeated every 4 weeks for 6 months. MRI images were acquired with a 1.5 = Tesla MR imager (Signa, GE Medical Systems, Milwaukee, gradient strength = 23 mT/m, slew rate = 120 mT/m/ms). Subjects were imaged in supine position with electrocardiogram (ECG) leads for cardiac gating and 5-inch circular surface coil on the chest. After acquiring coronal and axial fast cine MRI images, vertical long-axis images of the left ventricle were obtained. On these scout MRI images, a coronary arterial stent produces an area of signal attenuation (Fig. 1). Fast velocity-encoded cine MRI images were acquired in a double oblique imaging plane that was perpendicular to the LAD artery, with a slice thickness of 5 mm, a repetition time of 15 ms and an echo time of 5 ms, a field of view of 24 × 18 cm, a reconstructed image matrix of 256 × 128, a velocity window of ±100 cm/s, phase encoding steps of 96, views per segment of 4, and a sequential sampling in *k*-space. The two corresponding velocity encoding gradients were acquired within a cardiac cycle. The true temporal resolu-

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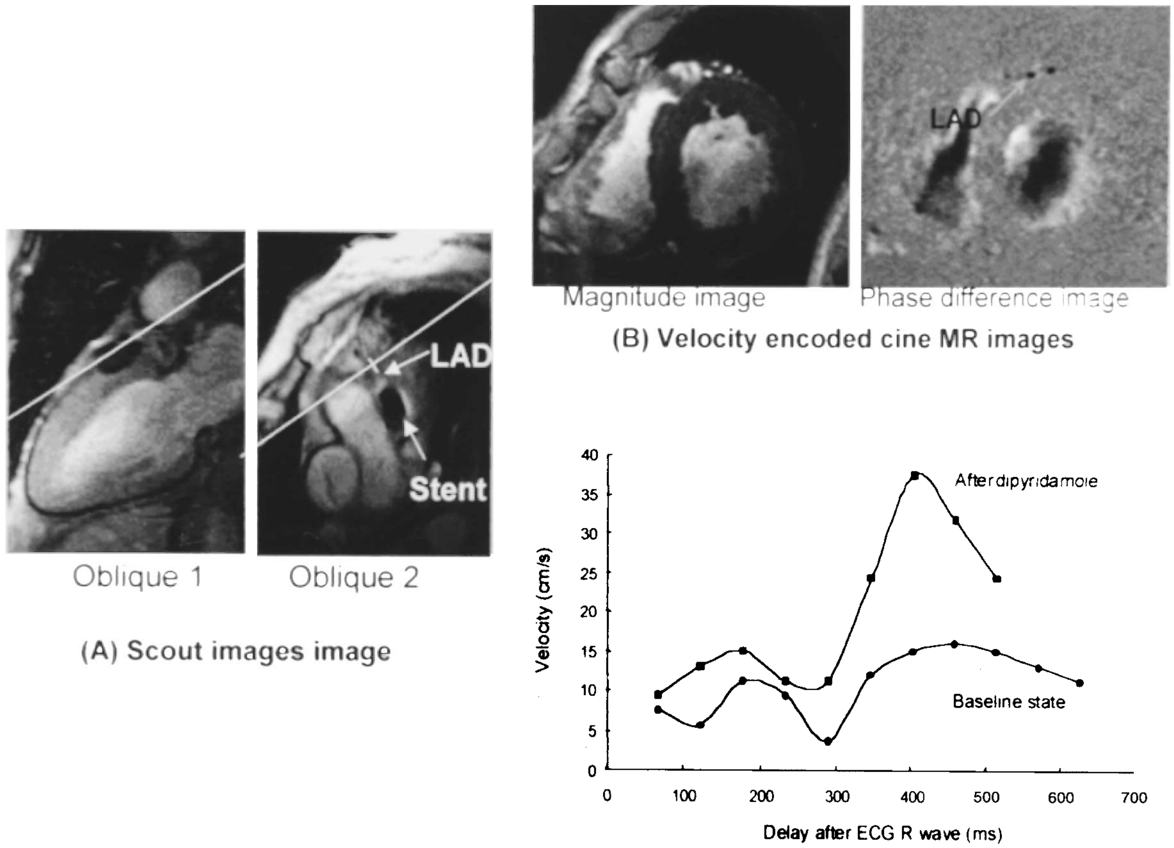

Figure 1. Definition of slice location for MRI blood flow measurements in the LAD artery on double oblique scout MRI images (A), magnitude and phase-difference images acquired with fast velocity-encoded cine MRI acquisition (B), and MRI blood flow velocity curves in the LAD artery before and after intravenous injection of dipyridamole (C).

tion of velocity-encoded cine MRI image acquisition was 120 ms. Magnitude and phase-difference velocity-encoded cine MRI images with 9 to 16 temporal phases were obtained with a view sharing reconstruction (9–10). Fat saturation pulse was not used in this study. Blood flow velocity at 1.5 cm distal to the stent was measured during a single breath-hold time for approximately 25 s. After measuring the baseline flow velocity, 0.56 mg/kg of dipyridamole was injected into the antecubital vein over 4 min. Stress velocity-encoded cine MRI images were obtained 2 min after finishing the dipyridamole injection. The total MRI procedure required approximately 45 min. MRI images were analyzed by placing a small region of interest (ROI) consisting of 2×2 pixels in LAD arterial lumen, and large ROI (30–50 pixels) on myocardium adjacent to LAD artery. Corrected blood flow velocity in the LAD artery in comparison to the adjacent myocardium was calculated. The coronary flow velocity reserve ratio was defined as a ratio of hyperemic to the baseline diastolic peak velocities (10).

All values are expressed as mean ± standard deviation. An unpaired 2-tailed t-test was used to compare differences in the flow velocity reserve ratios between two groups; a paired 2-tailed *t*-test was used to compare the serial changes in the flow velocity reserve ratios within the same group. A p value of <0.05 was considered statistically significant.

RESULTS

At follow-up angiography after 6 months, three patients showed significant (>50% luminal diameter) coronary restenosis (group 1) and the remaining seven pa-

Table 1

Clinical Characteristics and Angiographic Findings of the Study Population

	Group 1 ($n = 3$)	Group 2 ($n = 7$)	p value
Age (year)	63 ± 7	59 ± 10	NS
Men, Women	2, 1	4, 3	NS
Cardiac catheter			
LV systolic pressure (mm Hg)	139 ± 3	123 ± 22	NS
LV end diastolic pressure (mm Hg)	12.7 ± 4.9	10.3 ± 4.9	NS
LV ejection fraction (%)	63 ± 13	62 ± 9	NS
Stent size (mm)	3.5 ± 0.0	3.1 ± 0.5	NS
Angiographic result			
Stenosis (%) before procedure	86 ± 6	84 ± 10	NS
Stenosis (%) after stenting	5.0 ± 8.7	14.2 ± 11.8	NS
Stenosis (%) at follow-up	66 ± 8	28 ± 7	<0.001

tients had no significant stenosis (group 2). Clinical characteristics and results at angiography in the two groups are summarized in Table 1. Figure 1 shows fast velocity-encoded cine MRI images and blood flow velocity curves in the baseline state and after dipyridamole administration in a patient without restenosis. MRI studies were successful before and after pharmacological stress in all patients. Serial change of MRI flow velocity reserve in the coronary artery distal to the stent is presented in Figure 2. In group 2, without restenosis, the coronary flow velocity reserve ratio remained normal during the 6-month follow-up time. The flow velocity reserve ratio was 2.31 ± 0.30 at 1 month and 2.52 ± 0.25 at 6 months after stent implantation (p = NS). In contrast, the flow velocity reserve ratio in group 1 showed a significant decrease after 4 months. The flow velocity reserve ratio was 2.26 ± 0.49 at 1 month and 1.52 ± 0.09 at 6 months after stent implantation ($p < 0.05$).

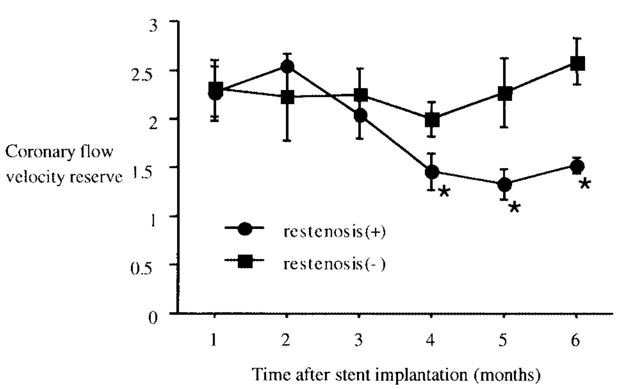

Figure 2. Serial changes of the coronary flow velocity reserve assessed with MRI in patients with restenosis and those without restenosis. * = $p < 0.05$ when compared with the coronary flow velocity reserve at 1 month.

DISCUSSION

In the current study, we demonstrated potential clinical usefulness of MRI for noninvasive prediction of restenosis after coronary interventions. Coronary flow reserve measurements have been used to assess the physiological significance of epicardial coronary stenosis and to evaluate the adequacy of revascularization following angioplasty and coronary artery bypass grafting (11–13). Wilson et al. (11) measured coronary flow reserve before, immediately after, and late after (7.5 months) balloon angioplasty using an intracoronary Doppler method. They found that coronary flow reserve immediately after dilatation may not reflect residual stenosis or eventual success of the angioplasty. However, late after angioplasty, all patients who developed restenosis had low coronary flow reserve, while all vessels without significant stenosis showed normal coronary flow reserve. The results of the current study are in agreement with this report.

While flow measurement with an intracoronary Doppler guide wire has already been established as a useful technique (14–15), it is invasive and is available only during cardiac catheterization. This has limited the widespread clinical use of intracoronary Doppler for functional assessment of the coronary artery after balloon angioplasty or stent implantation. MRI has a unique potential for noninvasive measurement of coronary blood flow and flow reserve. There are several potential sources of error in MRI assessment of coronary blood flow, such as partial volume averaging and motion blurring due to cardiac contraction. However, previous studies in animal models (16–17) and in humans (8–9) have documented an accurate quantification of blood flow and flow reserve using this technique. A recent study by Hundley et al. (18) also showed that noninvasive MRI measures of coronary flow reserve correlated well with similar measures obtained with the use of intracoronary Doppler flow wires, and that MRI measurement of coronary flow reserve had high sensitivity (100%) and specificity (83%) for identifying a stenosis >70% in the distal left main or proximal/middle LAD arteries.

The current study calculated the coronary flow reserve as the ratio of resting-to-stress coronary blood flow velocity instead of the ratio of actual flow volume. It is possible that the use of peak velocity and flow volume may give different values for coronary flow reserve, if the shape of the flow versus time curve and the diameter of the coronary artery are altered with stress. Flow volume measurement could be obtained by integrating the flow velocity and cross sectional area of the coronary artery over the cardiac cycle. However, for small vessels, the influence of partial volume averaging along the endothelial border of the coronary artery can be significant. Further improvements in the spatial resolution and temporal resolution of velocity-encoded cine MRI would be required to obtain an accurate assessment of coronary blood flow volume in the three major coronary arteries.

MRI assessment of coronary flow reserve does not eliminate the need for X-ray angiography when anginal symptoms or other noninvasive evidence of restenosis is encountered and coronary re-intervention is under consideration. However, this technique would be useful for detecting patients with silent ischemia in the coronary arterial territory after interventional procedures (19). In addition, when mild or intermediate restenosis is observed on X-ray angiography, MRI measurement of coronary flow reserve can be used to determine functional significance of the stenosis, and serial MRI studies can detect a gradual increase of the restenosis before onset of a severe or total occlusion.

In conclusion, significant reduction in coronary flow velocity reserve was documented with fast velocity-encoded cine MRI in patients with restenosis after stent implantation in the coronary arteries. The current study in a small number of patients shows the feasibility of this noninvasive method in demonstrating coronary restenosis after interventional procedure.

REFERENCES

1. Holmes, D.R. Jr.; Vliestra, R.E.; Smith, H.C.; Vetrovec, G.W.; Kent, K.M.; Cowley, M.J.; et al. Restenosis after Percutaneous Transluminal Coronary Angioplasty (PTCA): A Report from the PTCA Registry of the National Heart, Lung, and Blood Institute. Am. J. Cardiol. **1984**, *53*, 77c–81c.
2. Gruentig, A.R.; King, S.B. III; Schlumpf, M.; Siegenthaler, W. Long-Term Follow-Up after Percutaneous Transluminal Coronary Angioplasty: The Early Zurich Experience. N. Engl. J. Med. **1987**, *316*, 1127–32.
3. Nobuyoshi, M.; Kimura, T.; Nosakam, H.; Mioka, S.; Ueno, K.; Yokoim, H; et al. Restenosis after Successful Percutaneous Transluminal Coronary Angioplasty: Serial Angiographic Follow-Up Of 229 Patients. J. Am. Coll. Cardiol. **1988**, *12*, 616–23.
4. Hirshfeld, J.W. Jr.; Schwartz, J.S.; Jugo, R.; MacDonald, R.G.; Goldberg, S.; Savage, M.P.; Bass, T.A.; Vetrovec, G.; Cowley, M.; Taussig, A.S.; Whitworth, H.B.; Margolis, J.R.; Hill, J.A.; Pepine, C.J.; and the M-HEART investigators. Restenosis after Coronary Angioplasty: A Multivariate Statistical Model to Relate Lesion and Procedure Variables to Restenosis. J. Am. Coll. Cardiol. **1991**, *18*, 647–56.
5. Serruys, P.W.; de Jaegere, P.; Kiemeneij, F.; Macaya, C.; Rutsch, W.; Heyndrickx, G.; Emanuelsson, H.; Marco, J.; Legrand, V.; Materne, P.; Belardi, J.; Sigwart, U.; Colombo, A.; Goy, J.J.; van den Heuval, P.; Delcan, J.; Morel, M. A Comparison of Balloon-Expandable-Stent Implantation with Balloon Angioplasty in Patients with Coronary Artery Disease. N. Engl. J. Med. **1994**, *331*, 489–95.
6. Fischman, D.L.; Leon, M.B.; Baim, D.S.; Schatz, R.A.; Savage, M.P.; Penn, I.; Detre, K.; Veltri, L.; Ricci, D.; Nobuyoshi, M.; Cleman, M.; Heuser, R.; Almond, D.; Teirstein, P.S.; Fish, R.D.; Colombo, A.; Brinker, J.; Moses, J.; Shaknovich, A.; Hirshfeld, J.; Bailey, S.; Ellis, S.; Rake, R.; Goldberg, S. A Randomized Comparison of Coronary-Stent Placement and Balloon Angioplasty in the Treatment of Coronary Artery Disease. N. Engl. J. Med. **1994**, *331*, 496–501.
7. Gould, K.; Lipscomb, K.; Hamilton, G. Physiological Basis for Assessing Critical Coronary Stenosis. Am. J. Cardiol. **1974**, *33*, 87–94.
8. Hundley, W.G.; Lange, R.A.; Clarke, G.D.; Meshack, B.M.; Payne, J.; Landau, C.; McColl, R.; Sayad, D.E.;

Willett, D.L.; Willard, J.E.; Hillis, L.D.; Peshock, R.M. Assessment of Coronary Arterial Flow and Flow Reserve in Humans with Magnetic Resonance Imaging. Circulation **1996,** *93,* 1502–1508.
9. Shibata, M,.; Sakuma, H.; Isaka, N.; Takeda, K.; Higgins, C.B.; Nakano, T. Assessment of Coronary Flow Reserve with Fast Cine Phase Contrast Magnetic Resonance Imaging: Comparison with Measurement by Doppler Guide Wire. J. Magn. Reson. Imaging **1999**, *10,* 563–68.
10. Sakuma, H.; Blake, L.M.; Amidon, T.M.; O'Sullivan, M.; Szolar, D.H.; Furber, A.P.; Bernstein, M.A.; Foo, T.K.; Higgins, C.B. Coronary Flow Reserve: Noninvasive Measurement in Humans with Breath-Hold Velocity-Encoded Cine MR Imaging. Radiology **1996**, *198*, 745–50.
11. Wilson, R.F,.; Johnson, M.J.; Marcus, M.L.; Aylward, P.E.; Skorton, D.J.; Collins, S.; White, C.W. The Effect of Coronary Angioplasty on Coronary Flow Reserve. Circulation **1988**, *77*, 873–85.
12. Van Liebergen, R.A.M.; Piek, J.J.; Koch, K.T.; de Winter, R.J.; Lie, K.I. Immediate and Long-Term Effect of Balloon Angioplasty or Stent Implantation on the Absolute and Relative Coronary Blood Flow Velocity Reserve. Circulation **1998**, *98*, 2133–40.
13. De Paulis, R.; Tomai, F.; Gaspardone, A.; Colagrande, L.; Nardi, P.; Ghini, A.; Versaci, F.; de Peppo, A.P.; Gioffre, P.A.; Chiariello, L. Coronary Flow Reserve Early and Late after Minimally Invasive Coronary Artery Bypass Grafting in Patients with Totally Occluded Left Anterior Descending Coronary Artery. J. Thorac. Cardiovasc. Surg. **1999**, *118*, 604–609.
14. Graham, S.P.; Cohen, M.D.; Hodgson, J.M. Estimation of Coronary Flow Reserve by Intracoronary Doppler Flow Probes and Digital Angiography. Cathet. Cardiovasc. Diagn. **1990**, *19*, 214–21.
15. Joye, J.D.; Schulman, D.S.; Lasorda, D.; Farah, T.; Donohue, B.C.; Reichek, N. Intracoronary Doppler Guide Wire Versus Stress Sigle-Photon Emission Computed Tomographic Thallium-201 Imaging in Assessment of Intermediate Coronary Stenoses. J. Am. Coll. Cardiol. **1994**, *24*, 940–47.
16. Clarke, G.D.; Eckels, R.; Chaney, C.; Smith, D.; Dittrich, J.; Hundley, W.G.; NessAiver, M.; Li, H.F.; Parkey, R.W.; Peshock, R.M. Measurement of Absolute Epicardial Coronary Artery Flow and Flow Reserve with Breath-Hold Cine Phase-Contrast Magnetic Resonance Imaging. Circulation **1995**, *91*, 2627–34.
17. Sakuma, H.; Saeed, M.; Takeda, K.; Wendland, M.F.; Schwitter, J.; Szolar, D.H.; Derugin, N.; Shimakawa, A.; Foo, T.K.F.; Higgins, C.B. Quantification of Coronary Arterial Volume Flow Rate Using Fast Velocity-Encoded Cine MR Imaging. AJR **1997**, *168*, 1363–67.
18. Hundley, W.G.; Hamilton, C.A.; Clarke, G.D.; Hillis, L.D.; Herrington, D.M.; Lange, R.A.; Applegate, R.J.; Thomas, M.S.; Payne, J.; Link, K.M.; Peshock, R.M. Visualization and Functional Assessment of Proximal and Middle Left Anterior Descending Coronary Stenoses in Humans with Magnetic Resonance Imaging. Circulation **1999**, *99*, 3248–54.
19. Hundley, W.G.; Hillis, L.D.; Hamilton, C.A.; Applegate, R.J.; Herrington, D.M.; Clarke, G.D.; Braden, G.A.; Thomas, M.S.; Lange, R.A.; Peshock, R.M.; Link, K.M. Assessment of Coronary Arterial Restenosis with Phase-Contrast Magnetic Resonance Imaging Measurements of Coronary Flow Reserve. Circulation **2000**, *101*, 2375–81.

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