J. Tokyo Med. Univ., **69**(1) : 55-63, 2011

Cardiac cell damage in hypertrophic cardiomyopathy evaluated by beta-methyl-branched fatty acid analogue, iodine-123-15-(*p*-iodophenyl)-3-(*R,S*)-methylpentadecanoic acid (BMIPP) myocardial fatty-acid imaging and late gadolinium-enhanced contrast magnetic resonance imaging : usefulness of combining the two techniques

Masafumi KAWADE, Kunihiko TERAOKA, Masaharu HIRANO, Yuko IGARASHI, Masao YAMADA, Taishiro CHIKAMORI, Kenji TAKAZAWA, Akira YAMASHINA

Department of Cardiology, Tokyo Medical University

Abstract

Background : Late gadolinium-enhanced (LGE) magnetic resonance imaging (MRI) has been found to be a highly valuable imaging modality for myocardial characterization in cases of hypertrophic cardiomyopathy (HCM). In addition, abnormalities of BMIPP uptake have also been recognized in HCM. In this study, we hypothesized that abnormalities of fatty acid uptake and metabolism may be detected before fibrosis can be recognized on cardiovascular MRI in patients with HCM.

Methods and Results : Twenty-four patients with HCM were examined by both BMIPP myocardial fatty acid imaging and LGE MRI, and the results of the two imaging methods were compared. BMIPP uptake abnormalities were recognized in 23 of the 24 HCM patients (95.8%) and 126 out of the 408 segments (30.9%) examined, and were most frequently located in the interventricular septum and anterior wall of the left ventricle, the inferior wall and apex of the heart. Areas of LGE were recognized in 18 of the 24 HCM patients (75%) and 50 of the 408 segments (12.2%) examined, and were most frequently located in the interventricular septum of the left ventricle. Double-positive results of both BMIPP uptake abnormalities and LGE were recognized in 18 of the 24 cases (75.0%) and 45 of the 408 segments (11.0%) examined. Double-positive results were noted most frequently in the interventricular septum of the left ventricle and the anterior wall.

Conclusion : The areas showing BMIPP uptake abnormalities were more extensive than those showing LGE on MRI. In addition, the positivity rate for BMIPP uptake abnormalities in areas showing LGE on MRI was considerably higher than that of LGE positivity in areas positive for BMIPP uptake abnormalities. These results are not contradictory to our hypothesis. Therefore, differences between the examination methods in terms of the extent and positivity rate in cases of HCM may be related to the stage of progression of the cardiac muscle cell damage in cases of HCM. Thus, the use of both examinations together might be useful in the evaluation of the stage of disease progression in cases of HCM.

Received February 10, 2010, Accepted October 21, 2010

Key words : Hypertrophic cardiomyopathy, Cardiac MRI, ^{123}I-BMIPP

Corresponding author : Kunihiko TERAOKA, Division of Cardiology, Hachioji Medical Center, Tokyo Medical University, 1163 Tatemachi, Hachioji, Tokyo 193-0998, Japan

TEL : +81426655611 FAX : +81426651796 E-mail : teraoka@tokyo-med.ac.jp

Introduction

Cardiovascular magnetic resonance imaging (MRI) has been reported as a useful imaging modality for observation of the cardiac morphology and has shown high reproducibility in cardiac function analyses. In addition, late gadolinium-enhanced (LGE) MRI has also been shown to be highly valuable for the detection of infarcted myocardium and the prediction of the post-infarct myocardium viability in cases of ischemic heart disease[1)2)]. Abnormalities have been reported to be observed at a high frequency on LGE-MRI in cases of hypertrophic cardiomyopathy (HCM). More recently, it was demonstrated that areas showing LGE on the MR images in these cases corresponded to areas of myocardial fibrosis as assessed by histopathological examination[3)]. On the other hand, BMIPP (^{123}I 15-(*p*-iodophenyl)-3-(*R,S*)-methylpentadecanoic acid) myocardial fatty acid imaging is a nuclear imaging modality used to evaluate changes of the fatty acid metabolism in myocardial cells. BMIPP uptake abnormalities are known to arise from disordered fatty acid metabolism in ischemic heart muscle[4)]. In addition, BMIPP uptake abnormalities have also been frequently recognized in cases of HCM, and in these cases also, the abnormalities are assumed to arise from disordered cardiac muscle cell fatty acid metabolism[5)]. While several mechanisms have been proposed to explain the pathogenesis of cardiac muscle cell damage in cases of HCM, no consensus has been arrived at[6)]. Reports comparing the results of LGE-MRI with those of BMIPP myocardial fatty acid imaging in cases of HCM are almost non-existent[7)]. We hypothesized that abnormalities of fatty acid uptake and metabolism as evaluated by BMIPP imaging may be detected even before fibrosis can be recognized as positive enhancement on LGE MR images in patients with HCM. Therefore, in this study, we compared the results of LGE-MRI with those of BMIPP myocardial fatty acid imaging in cases of HCM, and reviewed the usefulness of combining the two imaging methods to evaluate the stage of progression of cardiac muscle cell damage in cases of HCM.

Methods

Twenty-four patients (17 men and 7 women ; average age, 57.4±11.9 years) with hypertrophic cardiomyopathy participated in the study, and were examined by both BMIPP myocardial fatty acid imaging and LGE-MRI at Tokyo Medical University Hospital during the five-year period from April 2001 to April 2006. Both examinations were performed within one month of each other. Informed consent was obtained from all of the patients and/or their families for participation in the study.

Table 1 Patients' clinical characteristics

Age	57.4±11.9
Male/Female	17/7
symptoms	
dyspnea	8
chest pain	2
chest oppression	2
faintness	2
presyncope	1
none	9
Findings of MRI	
EDV (ml)	81.7±27.3
EF (%)	61.0±18.5
LV mass (g/m^2)	179.1±70.9
Holter ECG	
VT (+)/VT (−)	6/18
Findings of UCG	
A/E	1.17±0.44
Neurohormonal factors	
BNP (pg/ml)	208.7±247.6

CMR, cardiovascular magnetic resonance ; EDV, end-diastolic volume ; EF, ejection fraction ; LVM, Left ventricular mass ; ECG, electrocardiogram ; VT, ventricular tachycardia ; UCG, echocardiography ; A/E, atrial contraction wave/early diastolic wave

In all subjects, the cause of the myocardial hypertrophy was somewhat unclear, and the diagnosis of HCM was based on the presence of LV hypertrophy without cavity dilatation (maximum wall thickness ≥15 mm), as well as the absence of other cardiac or systemic disease capable of producing the degree of hypertrophy evident in each patient[8 10)]. In addition, coronary angiography revealed no coronary artery lesions in any of the patients, and secondary myocardial disease was ruled out through a myocardial biopsy. Old myocardial infarction, end-stage HCM, and apical hypertrophic cardiomyopathy were ruled out by careful history-taking. The subjects' clinical backgrounds are shown in Table 1. We reviewed the status of the areas that were negative on LGE-MRI but positive for BMIPP uptake abnormalities on SPECT ; the final decision of a positive or negative rating was reached through consensus among 3 independent cardiologists blinded to other study data.

BMIPP Myocardial Fatty Acid Imaging.

Myocardial fatty acid imaging was performed using a ^{123}I-BMIPP system (Nihon Mediphysics, Nishinomiya, Japan). After the patient had fasted overnight, 111MBq of ^{123}I-BMIPP was administered intravenously while the patient rested, and the imaging scans were acquired 20-30 min after the injection[11)]. Data were acquired with a 2- or 3-detector gamma camera equipped with a low-energy high-resolution parallel multi-hole collimator (Prism 2000XP or Prism 3000XP, Picker ; Cleveland,

OH, USA) for 180- or 360-degree arcs. Single-photon emission computed tomography (SPECT) images were reconstructed from the data by a data processor (Odyssey VP, Picker) equipped with a Butterworth filter and a ramp filter. Each non-gated SPECT image was evaluated visually by 3 experts blinded to the clinical history and results of the LGE-MRI in the patients as positive or negative based on the presence absence of BMIPP uptake abnormalities. In the assessment of the SPECT images, a 17-segment model was used in accordance with the AHA Scientific Statement[11]. In the reconstitution of the 3 short-axis slices from the basal, middle and apical parts of the left ventricle, as well as in the long-axis images, we judged the degree of integration in the 17 segment model.

Cardiovascular MRI protocol

Cardiovascular MR imaging was performed with a Magnetom Avanto and Magnetom Symphony (Siemens, Erlangen, Germany, 1.5T whole-body MR system). A phased-array body coil and spine coil were used, with the subject in the supine position. After localizations, cine segmented balanced steady-state free precession images were acquired for long-axial, short-axial and 4-chamber views. The typical scan parameters are shown in Table 2. For each slice, single-slice imaging was acquired during a single breath-hold. In the long-axis view cine image, 8 to 10 slices of the short-axis view and 4-chamber view images were captured using the steady-state free precession method. The cardiac function analysis was input into the integral work station Argus together with 8-10 short-axis slices taken at intervals of 8 mm. LGE imaging was started 10 min after the intravenous administration of gadolinium-DTPA (0.15 mmol/kg, Magnevist, Japan Schering, Osaka, Japan). LGE images were acquired using the inversion-recovery segmented spoiled gradient-echo and phase-sensitive inversion recovery methods in long-axial, short-axial and 4-chamber views[12]. For each patient, the optimal inversion time was determined from the TI-Scout sequence which was executed immediately before the LGE imaging. To judge the presence or absence of LGE, we defined regions of interest (ROI) as large as possible in each segment of the myocardium and calculated the signal intensity in each segment. As a control, we measured the signal intensity of skeletal muscle at 17 points in the same film. The mean signal intensity of the skeletal muscle was 15.64±2.31. There are some papers in what the value of the signal intensity from non-infarct area is used as control to evaluate myocardial infarction area with LGE-MRI. However, in HCM a small amount of interstitical fibrosis, the area of which is not so hypertoropic is generally recognized. Therefore it is difficult to distinguish apparently normal areas from such areas with small amounts of interstitical fibrosis. We think that it is not suitable to employ myocardium as a control in HCM. Therefore we used the value of signal intensity from skeletal muscles as the control in this study. As in a previous report[13], we defined a mean signal intensity of the value in the skeletal muscle +2 SD as the threshold value, and defined any segment of myocardium with a signal intensity higher than this threshold as LGE-positive. The mean signal intensity in the LGE-positive segments was 46.1±31.3, while that in the LGE-negative segments was 12.9±5.3, indicating a significant difference between the two ($P<3.55\times10^{-6}$).

Table 2 Typical scan parameters of Cine MRI and LGE-MRI

	Cine	LGE
Method	steady-state free precession	spoiled gradient-echo
Bandwidth	930 Hz/pixl	130 Hz/pixl
TE	1.13 ms	4.18 ms
TR	2.26 ms	16.32 ms
Flip angle	70°	30°
FOV	340 mm×87.5%	340 mm×87.5
Image matrix	192×168	256×179
Voxel size	1.8×1.8 mm	1.7×1.3 mm
Slice thickness	8 mm	8 mm

The assessment of the presence or absence of LGE was conducted in 17 segments in a similar manner to that in the BMIPP myocardial fatty acid imaging.

Continuous data were presented as the average±standard deviation. Paired *t*-tests were performed to evaluate the differences between groups. Differences with a *P* value of <0.05 were considered to be statistically significant. The study protocol was approved by the ethics committee of our institution, and informed consent was obtained from each patient.

Results

1) Frequency of reduced BMIPP uptake (BMIPP-positive)

We determined that 23 of the 24 HCM patients were BMIPP-positive (95.8%). BMIPP uptake abnormalities were recognized in 126 out of the 408 segments (30.9%) examined, and most frequently in the interventricular septum of the left ventricle and anterior wall (segments 1, 2, 3, 7, 8, 13), the inferior wall (segments 4, 10, 15) and the apex of the heart (segment 17). The distribution of the BMIPP uptake abnormalities in the 17-segment model is illustrated in Fig. 1.

2) Frequency of enhancement on LGE-contrast MRI (LGE-positive)

We recognized LGE-positive areas in 18 of the 24 HCM patients (75%). Enhancement was recognized in 50 of the 408 segments (12.2%) examined, most frequently in the interventricular septum of the left ventricle

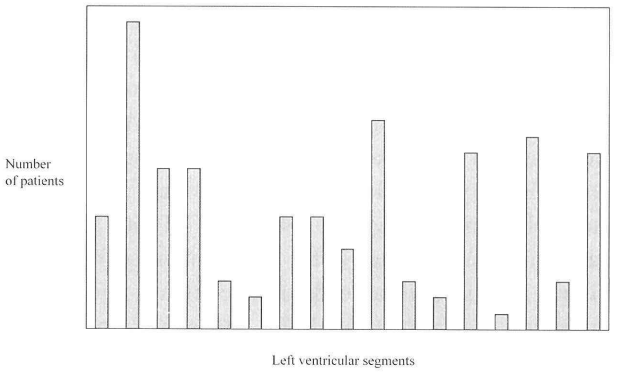

Fig. 1 Distribution of the BMIPP uptake abnormalities in the 17-segment model.

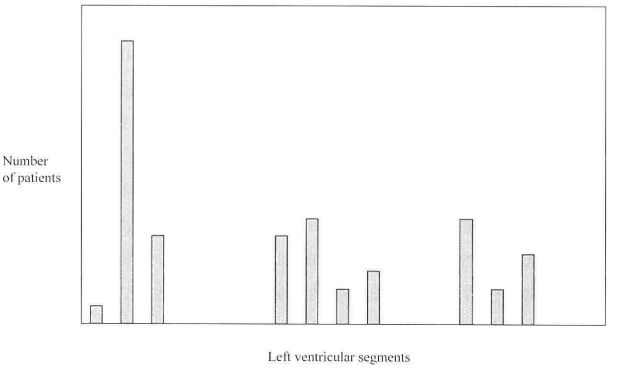

Fig. 2 Distribution of LGE in the 17-segment model.

(segments 2,8,14). The distribution of LGE in the 17-segment model is shown in Fig. 2.

3) Comparison of the distribution between BMIPP uptake abnormalities and LGE on MRI.

(a) Patients and segments that were both BMIPP-positive and LGE-positive. (Fig. 3)

Areas that were both BMIPP-positive and LGE-positive were recognized in 18 of 24 cases (75.0%) and 45 of all the 408 segments (11.0%) examined. Double positivity was recognized most frequently in the interventricular septum of the left ventricle (segments 2, 8 and 9) and the anterior wall (segments 7 and 13) (Fig. 4).

(b) Patients and segments that were both BMIPP-positive and LGE-negative. (Fig. 5)

Twenty-one of the 24 cases (87.5%) and 80 of the 408 segments examined (19.6%) showed a combination of BMIPP positivity and LGE negativity. Such BMIPP positive and LGE negative findings were most frequently located in the inferior wall (segments 4, 10, and 15) and the apex of the left ventricle (segment 17) (Fig. 6).

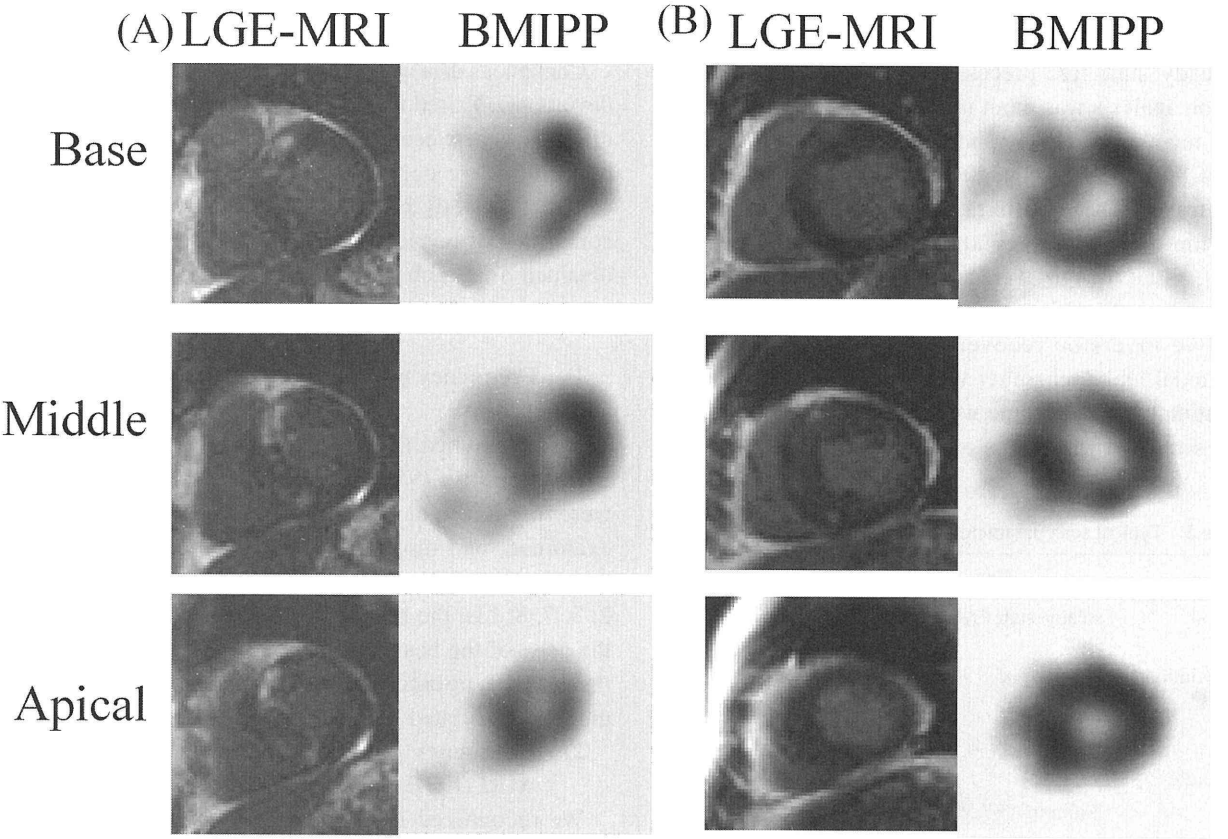

Fig. 3 (A) ; 63-year-old woman, (B) ; 56-year-old woman.
Three short-axial images of LGE and BMIPP are shown. Double positive findings (BMIPP uptake abnormalities+enhancement on LGE-MRI) were recognized.

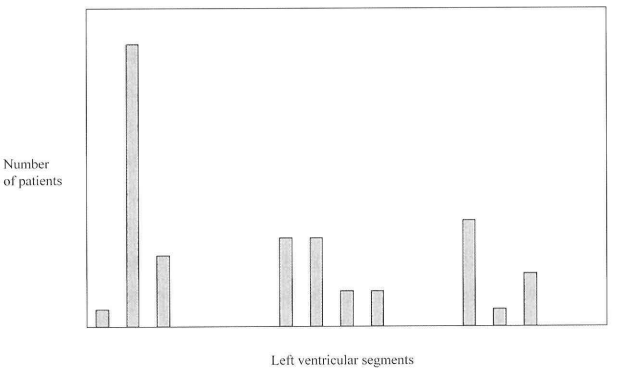

Fig. 4 Distribution of the areas showing both of BMIPP uptake abnormalities and LGE in the 17-segment model.

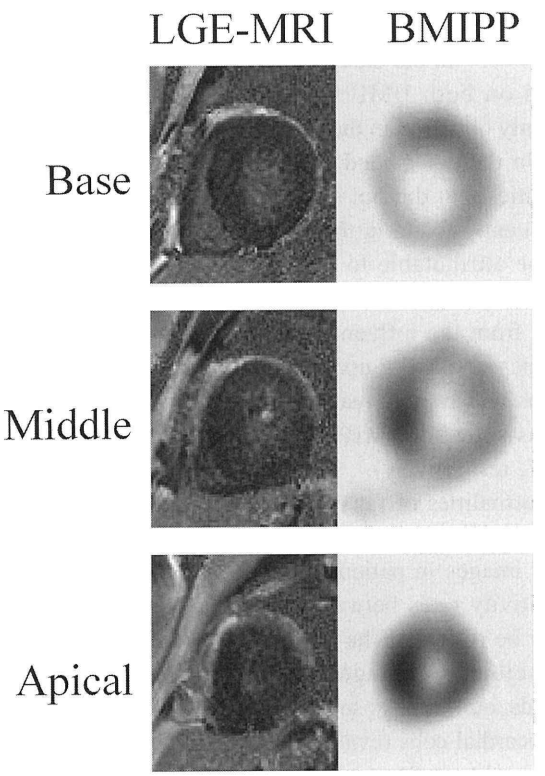

Fig. 5 43-year-old woman.
Positive BMIPP uptake abnormalities seen in areas showing negative enhancement on LGE-MRI.

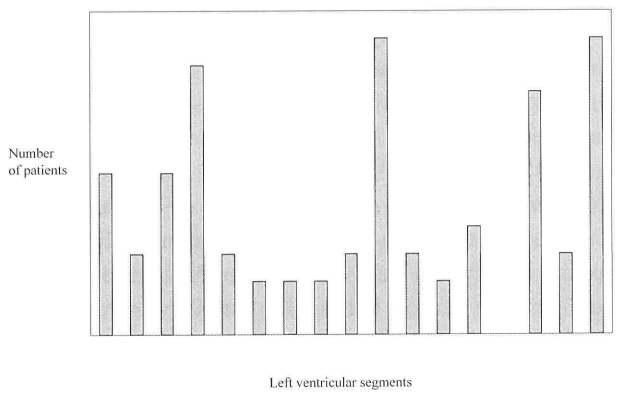

Fig. 6 Distribution of the areas showing BMIPP uptake abnormalities but no LGE in the 17-segment model.

(c) Patients and segments that were BMIPP-negative (normal BMIPP uptake) and LGE-positive. (Fig. 7)

Two of the 24 patients (8.3%) and 5 of the 408 segments (1.3%) showed a combination of BMIPP negativity and LGE positivity. (Fig. 8)

(d) BMIPP-negative and LGE-negative.

A double-negative result, that is, both BMIPP-negative and LGE-negative, was seen in only one patient.

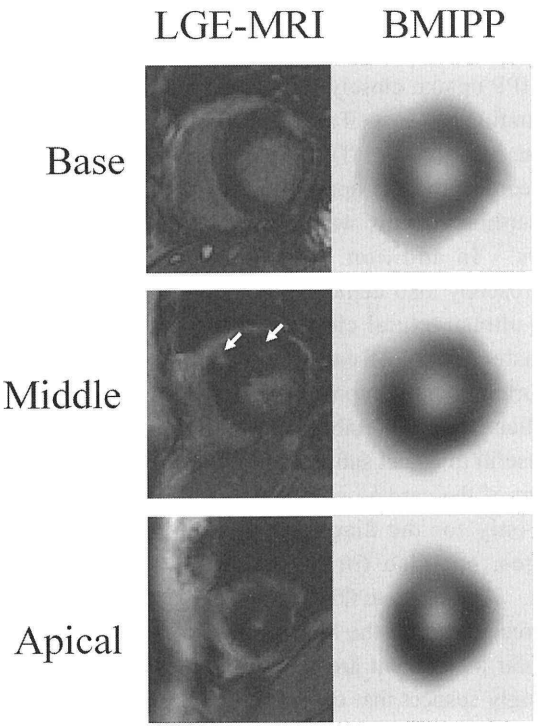

Fig. 7 48-year-old man.
Areas showing negative result on BMIPP myocardial fatty acid imaging but positive enhancement on LGE-MRI. The LGE-positive areas were extremely small, and detection of such small areas by SPECT may have been difficult. (Arrows)

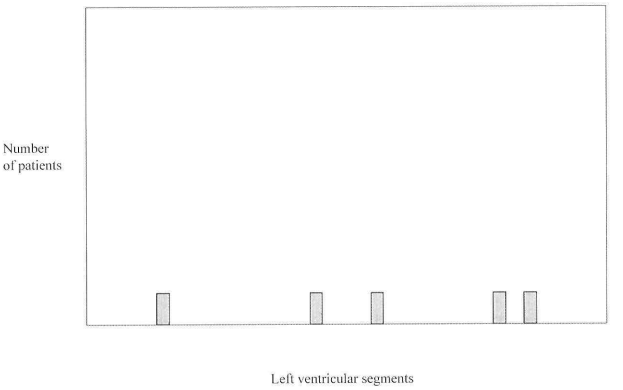

Fig. 8 Distribution of areas showing no BMIPP uptake abnormalities but LGE in the 17-segment model.

Discussion

In this study, areas showing BMIPP uptake abnormalities and enhancement on LGE-MR imaging were most frequently recognized in the interventricular septum in the HCM patients. However, the areas showing BMIPP uptake abnormalities were more extensive than those showing enhancement on the LGE-MR imaging. In addition, the frequency of BMIPP-positive cases was higher than that of LGE-positive cases.

In general, BMIPP uptake abnormalities are recognized at a high frequency in HCM patients ; this is presumed to be related to the disordered fatty acid metabolism in hypertrophic cardiac muscle cells[14-16]. BMIPP is a marker of metabolic alteration, because the degree of BMIPP uptake closely reflects the myocardial ATP concentration[17][18] as well as the mitochondrial and cell membrane functions[19]. Thet-Thet-Lwin et al[20] reported that the cardiac muscle uptake of BMIPP in a hamster model of cardiomyopathy was lower than that in normal hamsters. In addition, light microscopy and electron microscopy also demonstrated slight interstitial fibrosis and ultrastructural changes in the mitochondria in the hamster model of cardiomyopathy. Okazaki et al[21] reported using compartment model analysis for human cardiac BMIPP metabolism, that BMIPP SPECT might be useful to detect subtle changes in the fatty acid metabolism of the cardiac muscle cells in patients with HCM, not only for the diagnosis of HCM in its very early stages, but also for the evaluation of its progression. According to Ohtsuki, BMIPP uptake abnormalities are recognized at the highest frequency in the right ventricular attachment area and apex of the heart, and they strongly suspect that disordered fatty acid metabolism in cardiac muscle cells is prominent in these areas[15][16].

On the other hand, Kim reported, from a myocardial infarction experiment conducted using a canine model, that LGE-positive areas on MR imaging coincided with the infarct area determined histopathologically[1]. Subsequently, LGE-MRI was reported to be useful for evaluating the characteristics of myocardial infarct lesion and the viability of post-infarct myocardium[2]. On the other hand, in the case of HCM, LGE-positive areas on LGE-MRI are most often recognized at the site of right ventricle attachment of the interventricular septum. In addition, the extent of the LGE-positive area on LGE-MRI has been shown to positively correlate with the myocardial wall thickness, and negatively correlate with the percent thickening[22]. Furthermore, the extent of the LGE-positive areas on LGE-MRI has been recognized to be greater during the stages of disease progression than after the establishment of fibrosis, and also in cases with multiple risk factors for sudden cardiac death[23]. We had previously demonstrated that in patients with HCM, the LGE-positive areas on LGE-MRI were most frequently recognized at the right ventricle attachment area of the interventricular septum. We also demonstrated a decreased left-ventricular ejection fraction compared with that in cases with extensive LGE-positive areas on LGE-MRI. We also reported that the frequency of positive findings on LGE-MRI and the number of segments showing LGE positivity on LGE-MRI was greater in cases with ventricular tachycardiacs compared with that in those without ventricular tachycardia[13].

Kuribayashi et al reported, based on post-mortem examinations of hearts from HCM patients, that the characteristic histopathological changes, such as myocardial disarray and fibrosis, were most pronounced in the right ventricle attachment area of the interventricular septum[24][25]. In our study, double-positives (abnormal findings on both BMIPP imaging and LGE-MRI) were mainly observed in these same areas.

On the other hand, areas with BMIPP uptake abnormalities that did not show late enhancement were most frequently found in the inferior wall ; this is considered to be attributable to the influence of SPECT attenuation. In areas other than the inferior wall, i.e., areas distant from the influence of SPECT attenuation, the frequency of BMIPP uptake abnormalities in LGE-positive areas was much greater than that of LGE positivity in areas showing BMIPP uptake abnormalities (93% and 44%, respectively). In this study, we hypothesized that abnormalities of fatty acid uptake and metabolism may be detected before fibrosis can be recognized on LGE-MR images in patients with HCM. Difference in the positivity rates between the two examination methods may be related to the stage of progression of the cardiac muscle cell damage in cases with HCM. In other words, our findings suggest that the metabolic disorder in myocardial cells (evaluated by BMIPP) may be detected before the resultant histologic changes during the course of progression of the cardiac muscle cell damage in cases of HCM. This is consistent with our hypothesis.

On the other hand, 2 patients and 5 segments in the present study showed a combination of BMIPP negativity and LGE positivity. In both of the cases, the areas showing this combination of findings were extremely small, and detection of such small areas by SPECT might have been difficult. Wagner et al reported a diagnostic sensitivity of LGE-MRI and Tl cardiac-muscle SPECT for small subendocardial infarctions of 92% and 28%, respectively, and suggested that the extreme difference in spatial resolution between cardiac MRI and SPECT could be the reason behind the inability to recognize BMIPP uptake abnormalities in gadolinium enhancement-positive segments[26].

The differences in the frequency of positive findings between BMIPP fatty acid metabolic imaging and LGE-

MRI may reflect the stage of progression of the cardiac muscle cell damage in HCM. In cases with large differences in the positivity rates between the two imaging methods, cardiac muscle cell damage may be expected to occur in the future, and this damage can be assessed histologically. The results of our present study suggest that the combined use of the two imaging methods might yield important clinical information to allow identification of cases with a poor prognosis and to estimate the stage of progression of the disease. We further believe that we have demonstrated the importance of combining the *in vivo* findings of LGE-MRI and BMIPP fatty acid metabolic imaging for understanding the stages in the progression of the cardiac muscle abnormalities in HCM and the relevance of such information in the actual clinical situation.

However, it is necessary to prove this hypothesis with a large number of examples and longer follow up.

References

1) Kim RJ, Fieno DS, Parrish TB, Harris K, Chen E-L, Simonetti O, Bundy J, Finn JP, Klocke FJ, Judd RM : Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation **100** : 1992-2002, 1999
2) Choi KM, Kim RJ, Gubernikoff G, Vargas JD, Parker M, Judd RM : Transmural Extent of Acute Myocardial Infarction Predicts Long-Term Improvement in Contractile Function. Circulation **104** : 1101-1107, 2001
3) Kim RJ, Judd RM : Gadolinium-Enhancedmagnetic resonance imagingin hypertrophic cardiomyopathy : In vivo imaging of the pathologic substrate for premature cardiac death ? J Am Coll Cardiol **41** : 1568-1572, 2003
4) Tamaki N, Morita K, Kuge Y, Tsukamoto E : The role of fatty acids in cardiac imaging. J Nucl Med **41** : 1525-1534, 2000
5) Kobayashi H, Nakata T, Han S, Takahashi N, Hashimoto A, Tsuchihashi K, Nagao K, Tanaka S, Shimamoto K, Iimura O : Fatty acid metabolic and perfusion abnormalities in hypertrophied myocardium assessed by dual tracer tomography using thallium-201 and iodine-123-beta-methylpentadecanoic acid. J Cardiol **24** : 35-43, 1994
6) Varnava AM, Elliott PM, Sharma S, McKenna WJ, Davies MJ : Hypertrophic cardiomyopathy : the interrelation of disarray, fibrosis, and small vessel disease. Heart **84** : 476-482, 2000
7) Amano Y, Kumita S, Takayama M, Kumazaki T : Comparison of contrast-enhanced MRI with Iodine-123 BMIPP for detection of myocardial damage in hypertrophic cardiomyopathy. AJR **185** : 312-318, 2005
8) Maron BJ. Hypertrophic cardiomyopathy : a systematic review. JAMA **287** : 1308-1320, 2002
9) Maron BJ, McKenna WJ, Danielson GK, Kappenberger LJ, Kuhn HJ, Seidman CE, Shah PM, Spencer WH III, Spirito P, Ten Cate FJ, Wigle ED, Vogel RA, Abrams J, Bates ER, Brodie BR, Danias PG, Gregoratos G, Hlatky MA, Hochman JS, Kaul S, Lichtenberg RC, Lindner JR, O'rourke RA, Pohost GM, Schofield RS, Tracy CM, Winters WL Jr, Klein WW, Priori SG, Alonso-Garcia A, Blomström-Lundqvist C, De Backer G, Deckers J, Flather M, Hradec J, Oto A, Parkhomenko A, Silber S, Torbicki A : American College of Cardiology/European Society of Cardiology Clinical Expert Consensus Document on Hypertrophic Cardiomyopathy : a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. J Am Coll Cardiol **42** : 1687-1713, 2003
10) Klues HG, Schiffers A, Maron BJ. Phenotypic spectrum and patterns of left ventricular hypertrophy in hypertrophic cardiomyopathy : morphologic observations and significance as assessed by two-dimensional echocardiography in 600 patients. J Am Coll Cardiol **26** : 1699-1708, 1995
11) Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumberger JA, Ryan T, Verani MS : Standardized Myocardial Segmentation and Nomenclature for Tomographic Imaging of the Heart : A Statement for Healthcare Professionals From the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation **105** : 539-542, 2002
12) Kellman P, Arai AE, McVeigh ER, Aletras AH : Phase-Sensitive Inversion Recovery for detecting myocardial infarction using gadolinium-delayed hyperenhancement. Magnetic Resonance in Medicine **47** : 372-382, 2002
13) Teraoka K, Hirano M, Ookubo H, Sasaki K, Katsuyama H, Amino M, Abe Y, Yamashina A : Delayed contrast enhancement of MRI in hypertrophy cardiomyopathy. Magn Reson Imaging **22** : 155-161, 2004
14) Kurata C, Tawarahara K, Taguchi T, Aoshima S, Kobayashi A, Yamazaki N, Kawai H, Kaneko M : Myocardial emission computed tomography with iodine-123-labelled beta-methyl-branched fatty acid in patients with hypertrophic cardiomyopathy. J Nucl Med **33** : 6-13, 1992
15) Ohtsuki K, Sugihara H, Ito K, Matsumoto K, Taniguchi Y, Terada K, Nakagawa T, Shima T, Kuribayashi T, Ochiai M : The characteristic feature of myocardial imaging with 123I-labeled 15-(p-iodophenyl)-3R,S-methylpentadecanoic acid in hypertrophic cardiomyopathy with asymmetric septal hypertrophy. Kaku igaku **32** : 377-385, 1995
16) Ohtsuki K, Sugihara H, Umamoto I, Nakamura T, Nakagawa T, Nakagawa M : Clinical evaluation of

hypertrophic cardiomyopathy by myocardial scintigraphy using 123I-labelled 15- (p-iodophenyl)- 3-R, S-methylpentadecanoic acid (123I-BMIPP). Nucl Med Commun **15** : 441-447, 1994

17) Fujibayashi Y, Yonekura Y, Takemura Y, Wada K, Matsumoto K, Tamaki N, Yamamoto K, Konishi J, Yokoyama A : Myocardial accumulation of iodinated bata-methyl-branched fatty acid analogue, iodine-125-15-(p-iodophenyl)-3-(R,S)methylpentadecanoic acid (BMIPP), in relation to ATP concentration. J Nucl Med **31** : 1818-1822, 1990
18) Fujibayashi Y, Yonekura Y, Tamaki N, Yamamoto K, Som P, Knapp FF : Myocardial accumulation of BMIPP in relation to ATP concentration. Ann Nucl Med **7** (Suppl II) : s15-18, 1993
19) Ogata M : Myocardial uptake of 125I-BMIPP in rats treated with adriamycin. KAKUIGAKU **26** : 69-76, 1989
20) Thet-Thet-Lwin, Takeda T, Wu J, Tsuchiya Y, Itai Y : Abnormal retention of 99mTc-TF in a hamster model of cadiomyopathy analyzed by 125I-BMIPP autoradiography. Ann Nucl Med **18** : 195-202, 2004
21) Okizaki A, Shuke N, Sato J, Sasaki T, Hasebe N, Kikuchi K, Aburano T : A compartment model analysis for investigation of myocardial fatty acid metabolism in patients with hypertrophic cardiomyopathy. Nucl Med Commun **28** : 726-735, 2007
22) Choudhury L, Mahrholdt H, Wagner A, Choi KM, Elliott MD, Klocke FJ, Bonow RO, Judd RM, Kim RJ : Myocardial scarring in asymptomatic or mildly symptomatic patients with hypertorophic cardiomyopathy. J Am Coll Cardiol **40** : 2156-2164, 2002
23) Moon JCC, McKenna WJ, McCrohon JA, Elliott PM, Smith GC, Pennell DJ : Toward clinical risk assessment in hypertrophy cardiomyopathy with gadolinium cardiovascular magnetic resonance. J Am Coll Cardiol **41** : 1561-1567, 2003
24) Kuribayashi T, Roberts WC : Myocardial disarray at junction of ventricular septum and left and right ventricular free wall in hypertrophic cardiomyopathy. Am J Cardiol **70** : 1333-1340, 1992
25) Kuribayashi T : Spontaneus occurring hypertrophic cardiomyopathy in the rat. I. Pathologic features. Jpn Circ J **51** : 573-588, 1987
26) Wagner A, Mahrholdt H, Holly TA, Elliott MD, Regenfus M, Parker M, Klocke FJ, Bonow RO, Kim RJ, Judd RM : Contrast-enhanced MRI and routine single photon emission computed tomography (SPECT) perfusion imaging for detecting of subendocardial myocardial infarcts ; an imaging study. Lancet **361** : 374-379, 2003

肥大型心筋症の早期心筋障害に対するBMIPP心筋シンチと造影MRIの比較研究

川出昌史　寺岡邦彦　平野雅春
五十嵐祐子　山田昌央　近森大志郎
高沢謙二　山科章

東京医科大学内科学第二講座

【背景】 線維性組織はガドリニウム造影MRIにおいて、遅延造影を示す。一方、心筋細胞の脂肪酸代謝を画像化するBMIPP心筋シンチグラムは、肥大型心筋症においても、BMIPPの集積低下が、しばしば認められることが報告され、肥大型心筋症（HCM）においても、脂肪酸代謝障害が存在すること想定されている。HCMにおいて、BMIPP心筋シンチグラムで認める代謝障害は、遅延造影MRIで認められる線維化巣で生じているばかりでなく、線維化に至る背景を形成していることが推定される。

今回は、HCMにおけるBMIPP心筋シンチグラムと遅延造影MRIの所見を比較検討し、HCMの心筋細胞障害の進展およびその評価につき検討した。

【目的】 HCMにおいて、BMIPPスペクトおよび造影MRIにより検出される代謝異常と組織学的異常との関係を検討した。

【方法】 1か月以内にBMIPPスペクトおよび造影MRIを施行した24人のHCMを対象とした。乳頭筋レベルの左室短軸像を17分画し、それぞれの分画における、遅延造影とBMIPPの取り込み異常を比較検討した。

【結果】 1）BMIPP取り込み異常は、24例中23例（95.8%）、408分画中126分画に認められた（30.6%）。2）遅延造影は、24例中18例（75%）、408分画中50分画（12.2%）に認められた。3）(a) BMIPP集積低下と遅延造影がともに陽性であったのは24例中19例（79.2%）に認めた。分画では、全408分画中45分画（11.0%）であった。(b) BMIPPで集積低下かつGd-DTPA遅延造影は陰性であったのは24例中21例（87.5%）であった。分画では、全408分画中80分画（19.6%）であった。(c) ^{123}I-BMIPP集積低下陰性及びGd-DTPA遅延造影陽性は2例に認められた。分画では、全分画408分画中5分画（1.3%）に認めた。(d) 24例のHCMのうち、遅延造影、BMIPP取り込み異常のいずれも認めなかった例は1例のみであった（4.3%）。

【結語】 BMIPPにより検出されるHCMの早期心筋代謝異常は、造影MRIによる遅延造影によって検出される器質的異常に比して、より早期に生じている可能性があり、BMIPPと造影MRIによる遅延造影の両者を行うことはHCMの病期を判定する上で有用であると考えられた。

〈キーワード〉 肥大型心筋症、心臓MRI、^{123}I-BMIPP