Comparison of Myocardial ^{123}I-labeled fatty acid, 15-(p-iodophenyl)-3R,S-methylpentadecanoic acid (BMIPP) Uptake and Left Ventricular Function in Hypertrophic Cardiomyopathy

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Accepted for publication on September 9, 1996

ABSTRACT. A comparative study of myocardial ^{123}I-BMIPP uptake and left ventricular (LV) function in 17 cases with hypertrophic cardiomyopathy (HCM) was performed. Scintigrams using ^{123}I-BMIPP were obtained at 20 min and 2 hr after intravenous injection. The uptake ratio of the heart to upper mediastinum (H/M) in anterior planar images and the defect score (DS) in SPECT images were assessed. LV function was assessed by ECG-gated RI angiography using ^{99m}Tc-RBC. LV ejection fractions (EF) in a resting condition (EF_{Rest}) and during exercise stress (EF_{Ex}), and ΔEF ($=EF_{Ex}-EF_{Rest}$) as an index of LV functional reserve were also calculated. There were significant correlations between the DS and LV functional parameters, but there were no correlations between the ^{123}I-BMIPP uptake ratio and LV function. In conclusion, SPECT using ^{123}I-BMIPP proved to be useful in assessment of LV function and functional reserve in HCM.

Key words: ^{123}I-BMIPP — hypertrophic cardiomyopathy — LV function

Under normal aerobic conditions, fatty acid is mainly used as an energy source in the myocardium. Positron radiolabeled tracers, such as ^{11}C-palmitic acid, were developed to assess myocardial fatty acid metabolism. An in-hospital cyclotron is required to produce positron-emitting tracers with a very short half life. This has led to difficulties in performing clinical studies. Recently, ^{123}I-labeled fatty acid, 15-(p-iodophenyl)-3R,S-methylpentadecanoic acid (BMIPP) has been developed and supplied for conventional gamma camera imaging. ^{123}I-BMIPP has unique metabolic properties for the imaging of myocardial fatty acid utilization. In ischemic heart disease, reports that regions with left ventricular wall motion abnormalities exhibit decreased ^{123}I-BMIPP uptake, which suggesting that ^{123}I-BMIPP scintigraphy has the potential for detection of myocardial stunning and hibernation.[1-3] It has also been shown that cardiomyopathy without any myocardial perfusion abnormalities impairs ^{123}I-BMIPP uptake.[4,5] In contrast to findings in myocardial perfusion abnormalities, severely impaired ^{123}I-BMIPP uptake has been noted in hypertrophic cardiomyopathy (HCM).[6] Therefore, we

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hypothesized that myocardial fatty acid utilization in HCM would reflect left ventricular (LV) function and LV functional reserve under the condition of exercise. In this study, we compared myocardial ^{123}I-BMIPP uptake and LV function determined by RI angiographic studies.

METHODS

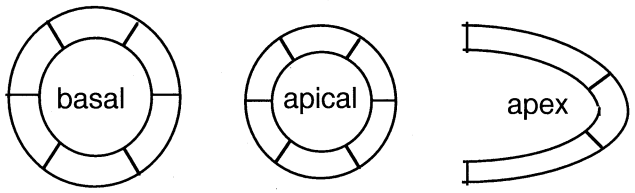
Subjects

^{123}I-BMIPP and Thallium scintigraphy and RI angiography were performed in 17 cases with HCM. Among these HCM cases were five cases with asymmetric septal hypertrophy (ASH), seven with apical hypertrophy (APH), two with diffuse hypertrophy, two with hypertrophic obstructive cardiomyopathy (HOCM) and one with the dilated phase of HCM. All patients were male, and the mean age was 59.2±9.2 years old (mean±s.d.).

BMIPP and Thallium Studies

^{123}I-BMIPP imaging was performed after intravenous injection of 148 MBq ^{123}I-BMIPP in a resting condition. Anterior chest planar images and myocardial SPECT were scintigraphied at 20 min and 2 hr after injection using a conventional gamma camera (GAMMAVIEW-T, Hitachi) equipped with a low energy, high resolution collimator. Anterior chest planar images were obtained with a preset time of 3 min. SPECT data were acquired over 180 degrees with 30 sec per 32 projections from right anterior to left posterior oblique views. The energy discrimination was centered on 159 keV with a 20% window. The reconstructed SPECT images were obtained from the acquisition data with smoothing and a Ramachandran filter. Within four weeks, myocardial perfusion imaging using ^{201}Thallium (^{201}Tl) was performed under a condition of resting or exercise stress, and SPECT images were obtained immediately and at 3 hr after ^{201}Tl injection.

To assess myocardial ^{123}I-BMIPP uptake, the uptake ratios of the heart to upper mediastinum (background) and myocardial ^{123}I-BMIPP washout rate using two anterior planar images with decay correction were calculated. SPECT images were visually assessed using uptake scores; LV was divided into 13 segments, using two short axis images and one vertical long axis image (Fig 1). ^{123}I-BMIPP uptake (Defect Score, DS) was the sum of the uptake score (0:



Total: 13 segments
0: normal, 1: slightly, 2: moderately,
3: severely reduced uptake

Fig 1. The defect score (DS) was the sum of the uptake score of the 13 segments shown in the figures above.

normal, 1: slightly, 2: moderately, 3: severely reduced uptake). In the assessment of ^{123}I-BMIPP uptake scores, myocardial perfusion images using ^{201}Tl were referred to as myocardial hypertrophy and fibrotic changes.

RI Angiographic Studies

To assess LV function, RI angiographies using *in vivo* labeled red blood cells (^{99m}Tc-RBC) were performed within four weeks. LV function was assessed by ECG-gated blood pool scintigraphy from a modified left oblique projection. Data were obtained with a sampling time of 30 msec, and these data were summed from 600 beats in a resting condition. After data acquisition in a resting condition, exercise was given using a supine bicycle ergometer. Data were acquired during exercise after the heart rate had become stable. Exercise stress was started with 25 or 50W, and was increased with 25W according to the symptom-limited method. From these data, the LV ejection fraction (EF) in a resting condition (EF_{Rest}) and LVEF at maximum exercise stress (EF_{Ex}) were calculated. Increase of EF from resting to max exercise stress, as the index of LV functional reserve, was calculated ($\Delta EF = EF_{Ex} - EF_{Rest}$). In a resting condition, the LV peak filling rate (PFR_{Rest}), as an index of the LV relaxation rate, was also calculated.

Data Analysis

^{123}I-BMIPP uptake and the LV functional parameters were compared. The linear regression lines were computed by the least squares method. A p value <0.05 was considered statistically significant.

RESULTS

A summary of the comparison of ^{123}I-BMIPP uptake and LV functional parameters is shown in Table 1.

TABLE 1. Correlation coefficients between ^{123}I-BMIPP uptake and left ventricular functional parameters

	EF_{Rest}	EF_{Ex}	ΔEF	PFR_{Rest}
DS_{20min}	−0.58*	−0.84+	−0.63+	−0.62*
DS_{2hr}	−0.44	−0.74+	−0.65+	−0.68+
H / M_{20min}	0.32	0.17	−0.17	0.13
H / M_{2hr}	0.20	0.30	0.23	0.36
washout rate	−0.02	−0.34	−0.57*	−0.32

* : $p<0.05$ + : $p<0.01$

(1) Defect Score and LV Function

Correlations are shown between DS and the LV functional parameters (Fig 2-4). Correlations between DS at 20 min and the LV functional parameters were all statistically significant. Correlation coefficients between DS at 20 min (DS_{20min}) and EF increased under the exercise stress condition (Rest: −0.58 to Ex: −0.84, Fig 2). Significant correlations between DS at 2 hr (DS_{2hr}) and EF_{Ex}, ΔEF, PFR_{Rest}, but not for EF_{Rest}, were obtained (Fig 4, Table 1).

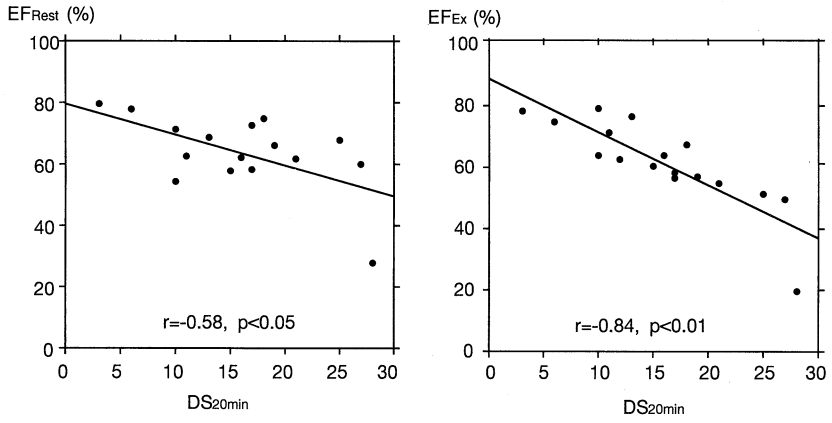


Fig 2. Correlation between DS20min and EFRest, EFEx

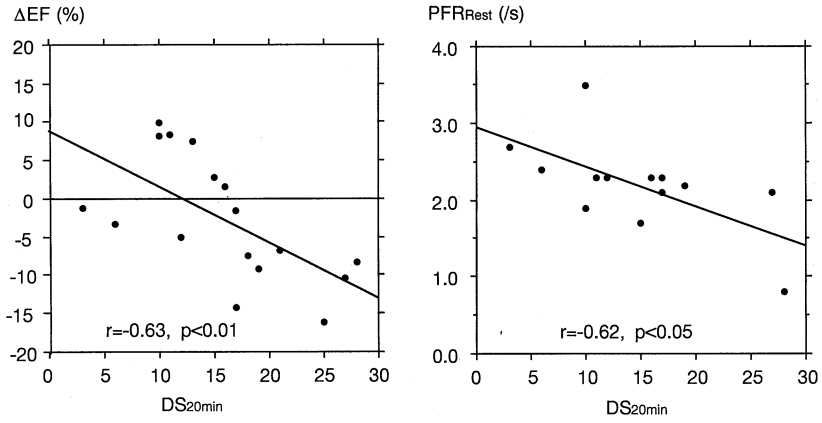


Fig 3. Correlation between DS20min and ΔEF, PFRRest

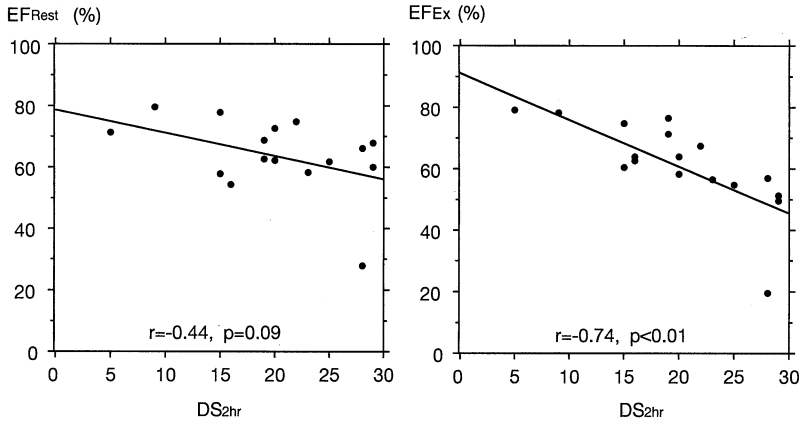


Fig 4. Correlation between DS2hr and EFRest, EFEx

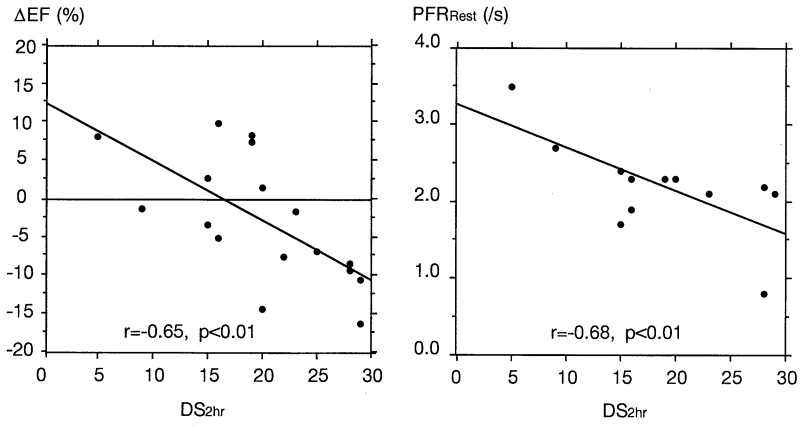


Fig 5. Correlation between DS2hr and ΔEF, PFRRest

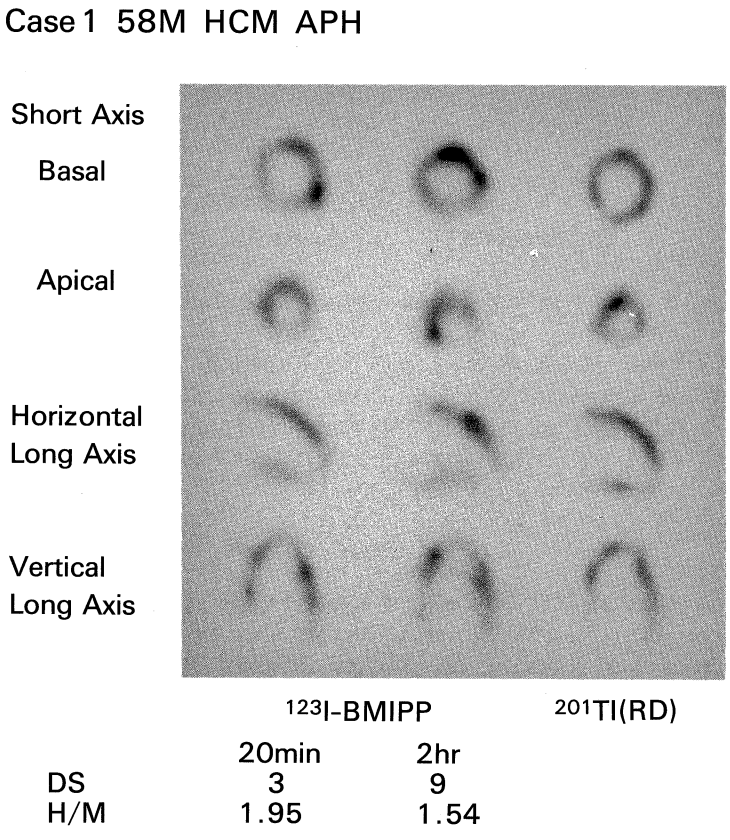


Fig 6. Case 1 (APH type) SPECTs using ^{123}I-BMIPP and ^{201}Tl

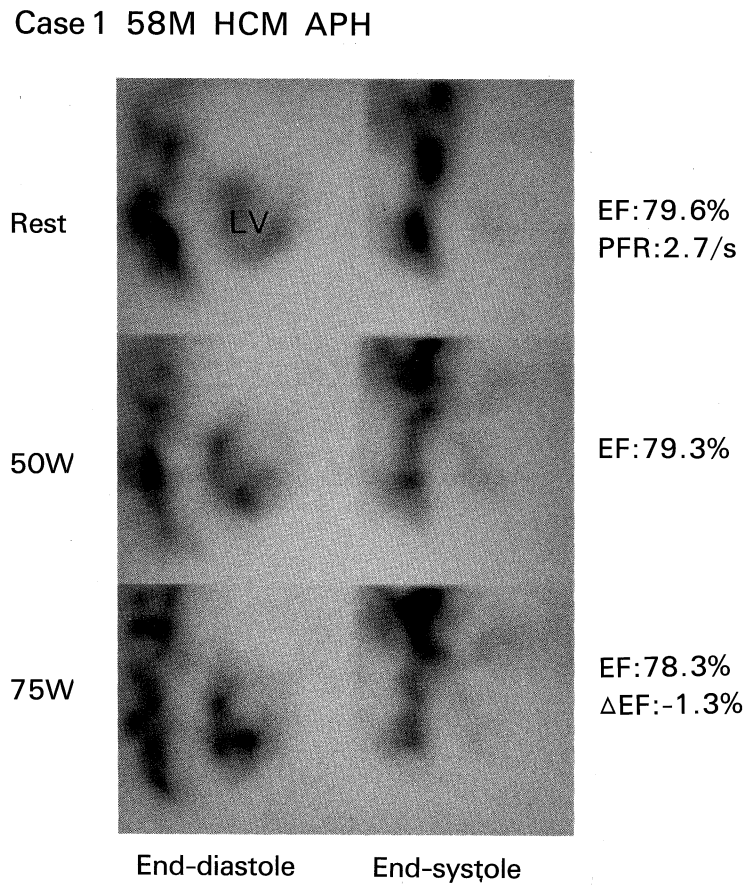


Fig 7. Case 1 (APH type) LV function assessed with RI angiography using ^{99m}Tc-RBC

(2) Uptake Ratio, Washout Rate and LV Function

There were no significant correlations between the ^{123}I-BMIPP uptake ratio at 20 min (H/M20min) and 2 hr (H/M2hr) and any of the LV functional parameters (Table 1). The correlation coefficient between the washout rate of ^{123}I-BMIPP and ΔEF was −0.57 (Table 1).

CASE PRESENTATION

Case 1. A case of HCM of apical hypertrophic type

No significant ^{123}I-BMIPP uptake abnormality was found, and the DS at 20 min and 2 hr was 3 and 4, respectively (Fig 6). LVEF at rest was 79.6%, indicating there was no change in EF under the exercise stress (Fig 7).

Case 2. A case of HCM of septal hypertrophic type

SPECTs using ^{123}I-BMIPP and ^{201}Tl are shown in Fig 8. Myocardial ^{123}I-BMIPP uptake was severely reduced. LVEF at rest was 60.1%, which was markedly decreased during exercise stress at the level of 75W, and ΔEF was −10.4% (Fig 9).

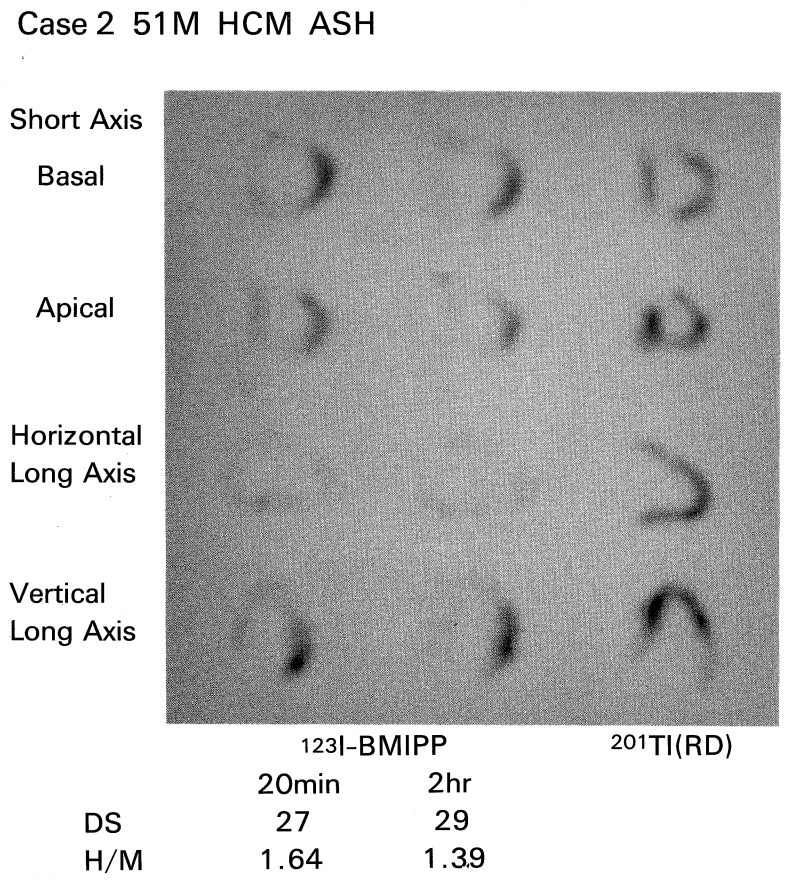


Fig 8. Case 2 (ASH type) SPECTs using ^{123}I-BMIPP and ^{201}Tl

DISCUSSION

Significant correlations between ^{123}I-BMIPP uptake and the left ventricular functional parameters have been shown. These findings seem to indicate that myocardial ^{123}I-BMIPP uptake might reflect LV function and LV functional reserve in HCM. In this study, ^{123}I-BMIPP uptake was assessed using the uptake ratio, washout rate and the defect score (DS) of SPECT images.[3,6] The myocardial uptake ratios of ^{123}I-BMIPP to the upper mediastinum did not correlate with LV function. In hypertrophic myocardium, as LV mass also increased, it might be necessary to correct myocardial fatty acid utilization by using LV mass or myocardial blood flow. There were no correlations between the ^{123}I-BMIPP uptake ratio and LV function in this study, because the uptake ratio of ^{123}I-BMIPP was not normalized by ^{201}Tl uptake. As the washout rate of ^{123}I-BMIPP from 20 min to 2 hr negatively correlated with ΔEF, this finding indicates that the kinetics of ^{123}I-BMIPP might be a useful indicator of LV functional reserve. In comparison of the DS and LV functional parameters, the DS at 20 min and 2 hr correlated with EF$_{Rest}$, EF$_{Ex}$ and ΔEF. It suspected that the DS at 20 min was sufficient to assess LV function and functional

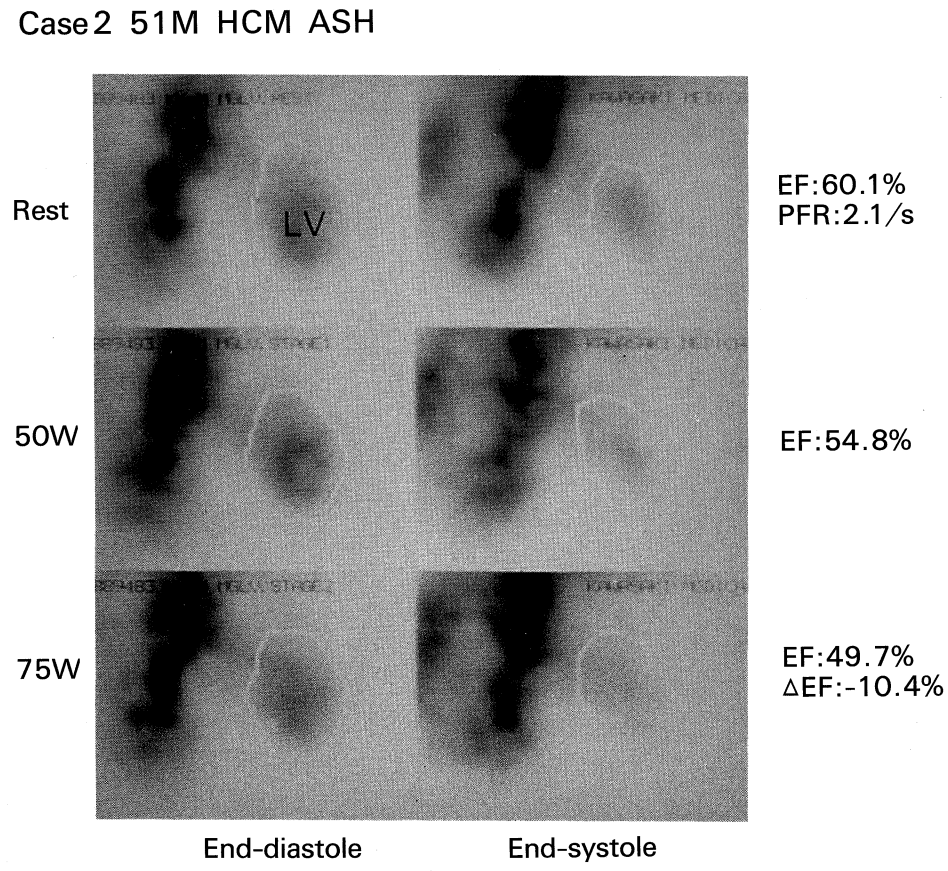


Fig 9. Case 2 (ASH type) LV function assessed with RI angiography using ^{99m}Tc-RBC

reserve in HCM. Good correlation between the DS and EFEx, as compared with EFRest, was shown, indicating that impaired ^{123}I-BMIPP uptake might reflect decreased LV functional reserve. There was significant correlation between the DS and PFRRest, suggesting that ^{123}I-BMIPP uptake might indicate the severity of HCM, which was characterized as impairment of LV diastolic dysfunction due to LV hypertrophic change. The mismatch of ^{123}I-BMIPP uptake and myocardial perfusion has been reported in HCM.[4-6] A method for quantifying ^{123}I-BMIPP uptake using myocardial perfusion in the hypertrophic heart is needed.

In conclusion, it was shown that the defect score of ^{123}I-BMIPP SPECT correlated significantly with the LV functional parameters, indicating that ^{123}I-BMIPP SPECT could be useful in the assessment of LV function and functional reserve in HCM.

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