Clinical Radiology 68 (2013) 676–682

Contents lists available at SciVerse ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Assessment of coronary microvascular dysfunction in hypertrophic cardiomyopathy: First-pass myocardial perfusion cardiovascular magnetic resonance imaging at 1.5 T

L. Huang [a], R. Han [a], T. Ai [a], Z. Sun [a], Y. Bai [b], Z. Cao [c], J.N. Morelli [d], L. Xia [a,*]

[a] *Department of Radiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China*
[b] *Department of Cardiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China*
[c] *Department of Epidemiology and Biostatistics, Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China*
[d] *Department of Radiology, Scott and White Hospital/Texas A&M Health Sciences Center, Temple, TX 76504, USA*

ARTICLE INFORMATION

Article history:
Received 22 October 2012
Received in revised form
26 December 2012
Accepted 9 January 2013

AIM: To evaluate the integrity of the coronary microvasculature in patients with hypertrophic cardiomyopathy (HCM) using first-pass magnetic resonance perfusion imaging.

MATERIALS AND METHODS: Twenty-two patients with HCM and 13 healthy volunteers underwent cardiac magnetic resonance imaging (CMR) at rest. Imaging protocols included short axis cine, first-pass myocardial perfusion, and late-phase contrast-enhanced imaging. Left ventricular end-diastolic wall thickness (EDTH), myocardial thickening, maximal upslope of time–intensity curve ($slope_{max}$), and late myocardial gadolinium enhancement (LGE) were assessed for each myocardial segment. The differences in $slope_{max}$, myocardial thickening, and EDTH between healthy volunteers and HCM patients were evaluated as were differences among hypertrophic segments of different severities (mild, moderate, and severe hypertrophy) in a one-way analysis of variance analysis. The differences in $slope_{max}$, myocardial thickening, and EDTH between the segments with and without LGE were compared by independent-sample *t*-test. A Pearson correlation test was used to determine the relationships between $slope_{max}$, EDTH, and myocardial thickening.

RESULTS: $Slope_{max}$ was statistically significantly less in HCM patients; the degree of myocardial thickening was also significantly reduced ($p < 0.001$). $Slope_{max}$ and the degree of thickening statistically significantly decreased with increasing degrees of myocardial hypertrophy ($p < 0.05$). Differences in $slope_{max}$, myocardial thickening, and EDTH were observed between segments with and without LGE ($p < 0.05$). $Slope_{max}$ and myocardial thickening were negatively correlated with EDTH.

CONCLUSION: First-pass myocardial perfusion CMR with $slope_{max}$ measurements demonstrates microvascular coronary dysfunction in patients with HCM, a determination that may aid in risk stratification, therapeutic planning, and determination of prognosis for HCM.

* Guarantor and correspondent: L. Xia, Department of Radiology, Tongji Hospital, 1095 Jiefang Avenue, Qiaokou District, Wuhan 430030, China. Tel.: +86 (0) 27 8366 3197; fax: +86 (0) 27 8366 2887.
E-mail address: xialiming88@yahoo.com.cn (L. Xia).

0009-9260/$ – see front matter © 2013 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.crad.2013.01.003

Introduction

Hypertrophic cardiomyopathy (HCM) is a genetic myocardial disease with multiple phenotypes, presenting with an array of clinical symptoms. Most HCM patients are asymptomatic in the early stages of the disease and are typically diagnosed by routine physical examination or familial screening. Symptoms of HCM range from palpitations, chest tightness, and chest pain.[1] Sudden cardiac death can also occur and has been associated with multiple clinical risk factors, such as microvascular coronary dysfunction and myocardial fibrosis.[2–4] Cardiac magnetic resonance imaging (CMR) is an increasingly utilized non-invasive imaging technique to study cardiovascular disease. Relative to single-photon-emission computed tomography (SPECT) and positron-emission tomography (PET), CMR provides both anatomical and functional information with excellent temporal and spatial resolution.[5,6] Myocardial perfusion studies using CMR with a bolus injection of gadolinium-based contrast agent have shown unique promise in the evaluation of microvascular ischaemic heart disease.[7] Few studies have investigated coronary microvascular dysfunction of the regional myocardium in HCM. The aim of the present study was to characterize myocardial microvascular function in patients with HCM with first-pass perfusion CMR. Conventional CMR and delayed contrast-enhanced MRI were also assessed in this cohort. The overall goal of this study was to achieve a greater understanding of HCM in order to aid cardiologists and radiologists in risk stratification of patients and selection of an appropriate therapeutic course.

Materials and methods

Patients and volunteers

Written informed consent was obtained from each participant in this institutional review board (IRB) approved study. Twenty-two patients with HCM (patient group) and 13 healthy volunteers (control group) were consecutively enrolled from April 2010 to November 2011 for clinical examination. The diagnosis of HCM was confirmed by Doppler echocardiography (17 asymmetric, two symmetric, and three apical cases of HCM). The inclusion criteria were: maximal left ventricle (LV) wall thickness ≥15 mm or ≥13 mm in patients with a family history of HCM and an absence of obvious extrinsic causes of left ventricular hypertrophy. Healthy volunteers were enrolled on the basis of a lack of any previous history of cardiovascular or other chronic disease, and did not regularly take any medications. Healthy volunteers with high blood pressure (>140/90 mmHg), an abnormal resting electrocardiogram (ECG), and/or an abnormal echocardiogram were excluded from this study.

MRI

All CMR examinations were performed on a 1.5 T MRI system (Signa HDxt, GE Healthcare, Milwaukee, Wisconsin, USA) with an eight-element phased-array coil. During MRI, retrospective ECG triggering was implemented. After acquisition of a scout image, two and four-chamber view cine imaging were acquired using a steady-state free precession (SSFP) sequence with breath-holding. Contiguous sections in the short-axis view were obtained from the atrioventricular valve to LV apex. Imaging parameters were: 3.7 ms repetition time (TR), 1.6 ms echo time (TE), 320 mm × 320 mm field of view (FOV), 224 × 192 matrix, 45° flip angle, 8 mm section thickness, 2 mm intersection gap, acceleration factor of 2, and an acquisition time per section of 8–10 s. A gadolinium chelate contrast agent [gadobenate dimeglumine (MultiHance),[8–10] 0.5 mmol/ml; Bracco, Milan, Italy] was then administered intravenously at a dose of 0.1 mmol/kg bodyweight and an injection rate of 3.5 ml/s, followed by a 12 ml saline flush injected at the same rate. Short-axis first-pass perfusion CMR was performed using a T1-weighted fast gradient-echo sequence with saturation-recovery magnetization preparation (FGRET). The parameters for perfusion imaging were: 7.6 ms TR, 2.4 ms TE, 360 mm × 270 mm FOV, 128 × 128 matrix, 25° flip angle, 8 mm section thickness, 2 mm intersection gap, and an acquisition time of approximately 1 min. After perfusion imaging, an additional dose of 0.1 mmol/kg bodyweight MultiHance was administered at a rate of 0.5 ml/s. Late gadolinium enhancement MRI images were acquired after a 15 min delay, utilizing an inversion-recovery prepared segmented gradient-echo sequence (MDE) with breath-holding. The orientations were short axis stack identical to cine and perfusion imaging. Imaging parameters were: 4 ms TR, 1.8 ms TE, 200–360 ms inversion time, 360 mm × 324 mm FOV, 192 × 160 matrix, 20° flip angle, 8 mm section thickness, 2 mm section gap, and an acquisition time per section of 16-20 s.

Image analysis

All image datasets were loaded into a dedicated off-line workstation. Standard post-processing software (Report-card Version 3.7, GE Healthcare) was utilized to calculate measures of LV function, myocardial perfusion, and late gadolinium enhancement (LGE). These measures were computed for each of the 16 myocardial segments defined by American Heart Association (AHA) guidelines.[11] These 16 segments (Fig 1) included the basal (anterior, antero-septal, infero-septal, inferior, infero-lateral and antero-lateral), mid-ventricular (anterior, antero-septal, infero-septal, inferior, infero-lateral and antero-lateral), and apical (anterior, septal, inferior and lateral) aspects of the heart. A total of 352 myocardial segments were evaluated in patient group versus 208 in the control group. All segments in the HCM patients were classified based on the left ventricular end-diastolic wall thickness (EDTH). A non-hypertrophic segment was defined as a segment with EDTH <15 mm, and a hypertrophic segment as a segment with EDTH ≥15 mm. The hypertrophic segments were further classified as mild (EDTH = 15–20 mm), moderate (EDTH = 20–25 mm), severe (EDTH = 25–30 mm), and very severe (EDTH >30 mm).

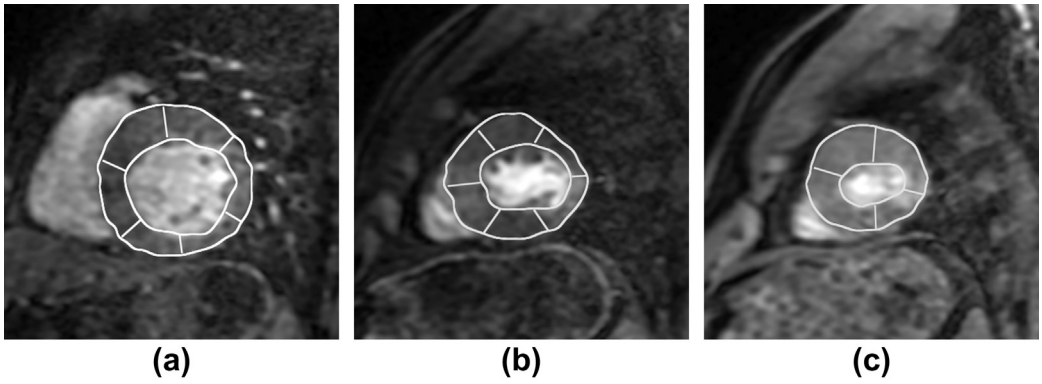

Figure 1 Segmentation of the LV on myocardial perfusion images demonstrating (a) six basal segments, (b) six mid segments, and (c) four apical segments.

On short-axis cine MRI images, the following LV functional parameters were measured and normalized to body surface area: LV end-diastolic volume index (ml/m^2), LV end-systolic volume index (ml/m^2), LV stroke volume index (ml/m^2), LV ejection fraction (LVEF; %), and LV mass index (g/m^2). EDTH and end-systolic wall thickness (ESTH) was also measured in all 16 segments for each case. The percentage of LV wall thickening was computed as:

$$\text{Thickening} = \frac{\text{ESTH} - \text{EDTH}}{\text{EDTH}} \times 100\%$$

On perfusion images, time–intensity curves were obtained for each myocardial segment in each subject group throughout the entire image acquisition. The maximal upslope (slope$_{max}$) of each myocardial segment, reflecting the microvascular function of the regional myocardium, was measured and normalized to the maximal upslope the time–intensity curve obtained within the LV cavity (%; Fig 2). LGE was defined as MRI signal intensity (SI) more than six standard deviations greater than the mean SI of myocardium in the same section.[12]

Statistical analysis

Results are given as mean ± SD (standard deviation). Statistical analysis was performed in SPSS 18 (PASW 18, SPSS, Chicago, IL, USA). A one-way analysis of variance (ANOVA) analysis was used to calculate the differences in slope$_{max}$, myocardial thickening, and EDTH between normal segments in healthy volunteers and both hypertrophic and non-hypertrophic segments in patients. Differences among patients with mild, moderate, and severe hypertrophy were also assessed in this manner. An independent-sample *t*-test was used to calculate differences in slope$_{max}$, myocardial thickening, and EDTH between hypertrophic segments with and without LGE. A Pearson correlation was utilized to determine relationships among slope$_{max}$, EDTH, and the degree of myocardial thickening. *p*-Values <0.05 were considered statistically significant.

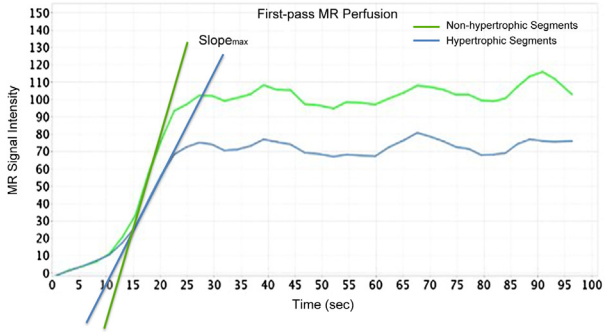

Figure 2 The time–intensity curve derived from myocardial perfusion images shows measurements of the slope$_{max}$ in hypertrophic and non-hypertrophic myocardial segments.

Results

Healthy volunteers (control group) and patients with HCM (patient group) differed in left ventricular ESV index, mass index, and LVEF but not in basic subject characteristics (i.e., age or gender) or in other functional parameters shown in Table 1. In the HCM group, 131 hypertrophic (37.2%) and 221 non-hypertrophic segments (62.8%) were identified. Of the hypertrophic segments, 97 (74.0%) were mild, 26 (19.8%) moderate, seven (5.3%) severe, and one (0.8%) very severe. Only one very severe segment was identified, and thus no statistical conclusions regarding this segment could be drawn. LGE was present in 25 myocardial segments in the HCM group and in no segments in the healthy volunteers. All segments with LGE were hypertrophic. Of the segments with LGE (Fig 3), the degree of hypertrophy was mild in 12 (of 97 mildly hypertrophic segments, 12.4%), moderate in six (of 26 moderately hypertrophic segments, 23.1%), severe in six (of seven severely hypertrophic segments, 85.7%), and very severe in one segment (of one very severely hypertrophic segment, 100%).

Calculations of slope$_{max}$, myocardial thickening, and EDTH in the healthy volunteer and HCM patients are provided in Table 2. Slope$_{max}$ measurements for both hypertrophic and non-hypertrophic subgroups in HCM patients were statistically significantly lower than for the control group ($p < 0.001$, Fig 4). Hypertrophic segments also

Table 1
General characteristics of the hypertrophic cardiomyopathy (HCM) patients and healthy volunteers with relevant associated functional parameters.

	HCM patients	Healthy volunteers	t	*p*-Value
Number (cases)	22	13	-	-
Age (years)	52.4 ± 12.5	46.6 ± 15.1	1.235	0.225
Male gender (%)	66.7	61.5	0.415	0.778
Weight (kg)	75.0 ± 10.7	69.7 ± 13.4	1.290	0.206
Body surface area (m^2)	1.85 ± 0.13	1.76 ± 0.16	1.823	0.077
Heart rate (beats/min)	70.4 ± 9.2	70.6 ± 12.0	0.057	0.955
LV EDV index (ml/m^2)	67.1 ± 23.3	70.8 ± 15.0	0.502	0.619
LV ESV index (ml/m^2)	18.3 ± 9.0	25.1 ± 6.2	2.400	0.022
LV SV index (ml/m^2)	44.8 ± 11.5	45.6 ± 10.3	0.205	0.839
LVEF (%)	73.0 ± 7.0	64.5 ± 5.3	3.771	0.001
LV mass index (g/m^2)	80.4 ± 51.1	35.7 ± 8.0	4.015	0.001

The values were expresses as mean ± SD. EDV, end-diastolic volume; ESV, end-systolic volume; LVEF, left ventricular ejection fraction.

demonstrated statistically significantly lower $slope_{max}$ than non-hypertrophic segments in HCM patients ($p < 0.001$, Fig 4). The degree of myocardial thickening in hypertrophic segments was statistically significantly less than in non-hypertrophic segments in HCM patients and less than those in normal volunteers ($p < 0.001$, Fig 4). However, there was no statistically significant difference in the degree of myocardial thickening between non-hypertrophic segments in the HCM group and normal segments of healthy volunteers ($p = 0.194$, Fig 4). Statistically significant differences in EDTH were observed among hypertrophic and non-hypertrophic segments in HCM patients and normal segments in healthy volunteers in pairwise comparisons ($p < 0.001$, Fig 5).

Table 2
$Slope_{max}$, degree of myocardial thickening, and EDTH among normal myocardial segments in healthy volunteers as well as non-hypertrophic and hypertrophic segments in the patient group.

	Normal segments	Non-hypertrophic segments	Hypertrophic segments	*p*-Value
N (segments)	208	221	131	-
$Slope_{max}$ (%)	63.4 ± 15.4	55.6 ± 18.6	46.8 ± 20.7	<0.001
Thickening (%)	89.8 ± 36.2	94.0 ± 34.9	53.2 ± 27.6	<0.001
EDTH (mm)	5.1 ± 1.4	6.8 ± 1.4	17.6 ± 3.9	<0.001

The values were expressed as mean ± SD. EDTH, end-diastolic wall thickness; N, the number of segments; $Slope_{max}$, maximal upslope of time–intensity curve.

The severity of the hypertrophic myocardial segments is shown in Table 3. The $slope_{max}$ of segments with mild

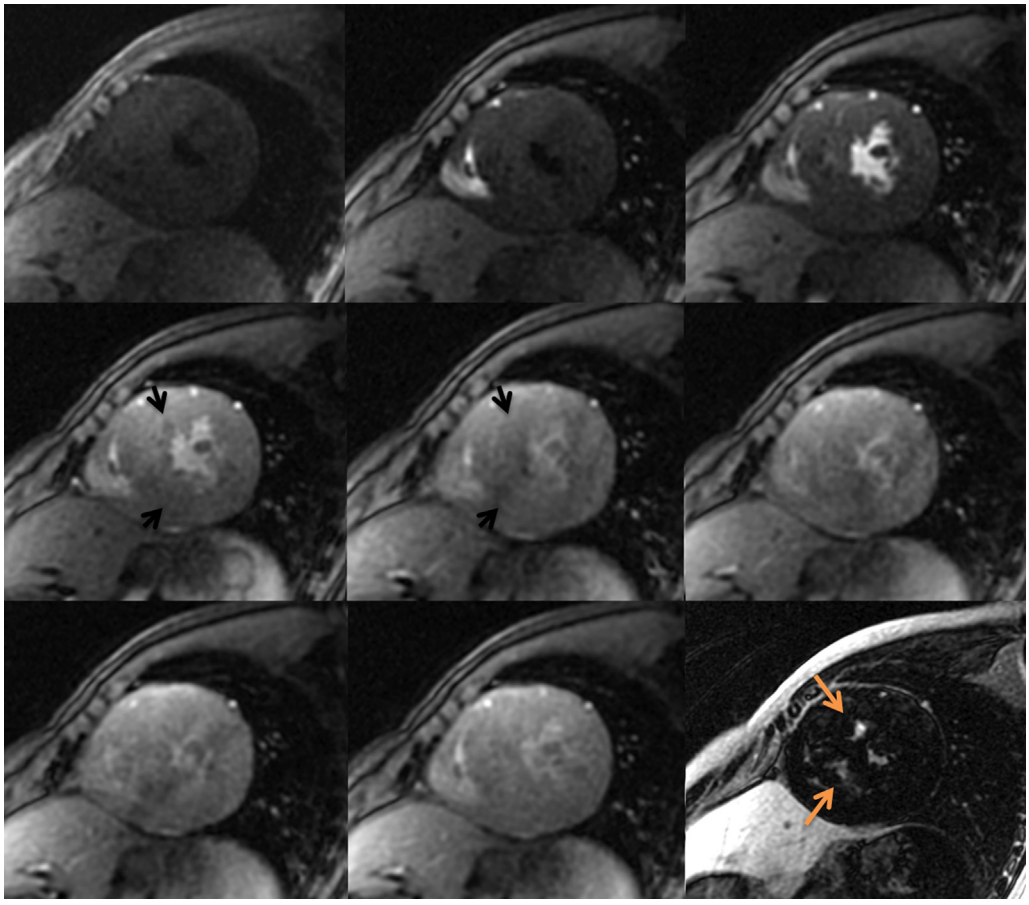

Figure 3 Myocardial perfusion examination demonstrating a perfusion defect in the antero-septal and infero-septal mid segments on images (black arrow) obtained pre-contrast and at 2.4, 12, 24, 36, 48, 60, and 72 s post-contrast medium administration. There are multi-focal, patchy areas of late gadolinium enhancement in the antero-septal and infero-septal mid myocardial segments on images (orange arrow) obtained after a 15 min delay.

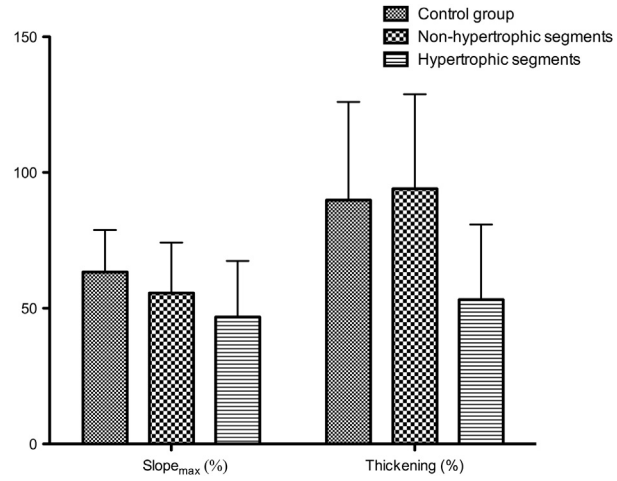

Figure 4 Comparisons of slope$_{max}$ and myocardial thickening in myocardial segments of normal volunteers versus non-hypertrophic and hypertrophic segments of HCM patients. There were statistically significant differences in slope$_{max}$ between each of these groups. Thickening of the hypertrophic myocardial segments was statistically significantly less than thickening of the other two segments. However, there was no significant difference in the degree of thickening between normal segments in control group and non-hypertrophic segments in patient group.

hypertrophy was statistically significantly greater than that of segments with moderate and severe hypertrophy ($p = 0.021$ and $p = 0.020$, Fig 6). No statistically significant differences in slope$_{max}$ were observed between segments with moderate and severe hypertrophy ($p = 0.495$, Fig 6). The degree of myocardial thickening was less in segments with mild and moderate hypertrophy than in segments with severe hypertrophy ($p < 0.001$ and $p = 0.002$, Fig 6). No statistically significant differences in myocardial thickening were observed between segments with mild and moderate hypertrophy ($p = 0.980$, Fig 6). Slope$_{max}$ and the degree of myocardial thickening were negatively correlated with

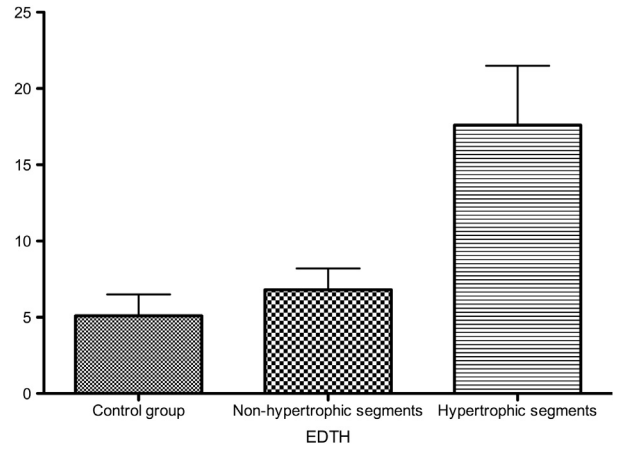

Figure 5 Comparisons of EDTH among myocardial segments in normal volunteers versus non-hypertrophic and hypertrophic segments in the HCM patients. There were statistically significant differences in EDTH between each of these groups.

Table 3
Slope$_{max}$, myocardial thickening and EDTH in myocardial segments with mild, moderate and severe hypertrophy.

	Mild hypertrophic segments	Moderate hypertrophic segments	Severe hypertrophic segments	*p*-Value
N (segments)	97	26	7	-
Slope$_{max}$ (%)	49.9 ± 22.0	40.3 ± 13.3	33.7 ± 11.1	0.022
Thickening (%)	55.7 ± 25.9	53.3 ± 31.8	23.9 ± 11.3	0.011

The values were expressed as mean ± SD. N, the number of segments; Slope$_{max}$, maximal upslope of time–intensity curve.

EDTH ($r = -0.264$, $p = 0.002$ and $r = -0.312$, $p < 0.001$, respectively).

All LGE appeared in mid wall of myocardial segments. Slope$_{max}$ and the degree of myocardial wall thickening were statistically significantly less in segments with LGE than in segments without LGE ($p < 0.05$, Table 4). The EDTH in segments with LGE was statistically significantly greater than in segments without ($p < 0.001$, Table 4).

Discussion

HCM is a common hereditary cardiomyopathy characterized by left ventricular hypertrophy without ventricular dilation. The main pathophysiological feature in HCM is adverse left ventricular myocardial remodelling, resulting in an increased mass index and reduced compliance with impaired ventricular relaxation.[13,14] CMR has the unique advantage of providing morphological, functional, and perfusion imaging within a single study. First-pass CMR

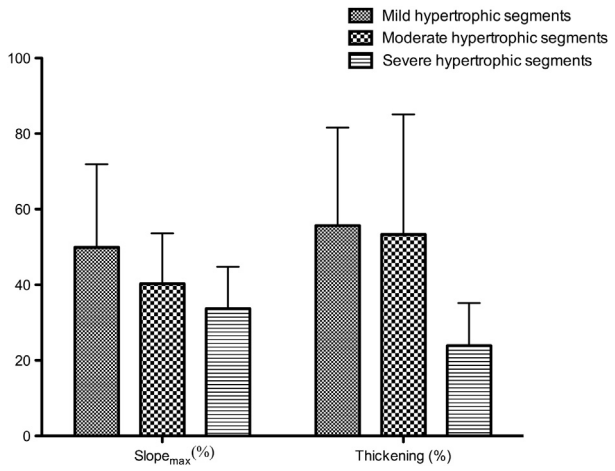

Figure 6 Comparisons of slope$_{max}$ and myocardial thickening among segments with mild, moderate, and severe hypertrophy. The slope$_{max}$ of the segments with mild hypertrophy was statistically significantly greater those of segments with moderate and severe hypertrophy. There was no significant difference in slope$_{max}$ between segments with moderate and severe hypertrophy. The degree of myocardial thickening of segments with severe hypertrophy was statistically significantly less relative to segments with mild and moderate hypertrophy. However, the latter two groups demonstrated no statistically significant differences in terms of the degree of myocardial thickening.

Table 4
$Slope_{max}$, myocardial thickening, and EDTH in hypertrophic myocardial segments with and without late gadolinium enhancement

	LGE segments	Non-LGE segments	*p-Value*
N (segments)	25	106	-
$Slope_{max}$ (%)	30.5 ± 10.6	50.7 ± 20.7	<0.001
Thickening (%)	41.3 ± 25.0	56.4 ± 27.5	0.013
EDTH (mm)	21.4 ± 4.8 mm	16.7 ± 3.1 mm	<0.001

The values were expressed as mean ± SD. EDTH, end-diastolic wall thickness; LGE, delay gadolinium enhancement; N, the number of segments; $Slope_{max}$, maximal upslope of time–intensity curve.

perfusion can be used to evaluate myocardial microvascular dysfunction in different heart diseases by measuring myocardial blood flow (MBF), maximal upslope of the time–intensity curve, perfusion reserve, and other parameters.[4,15] Utilization of perfusion parameters in combination with other functional and anatomical measures, such as wall thickening, wall thickness, and LGE, may facilitate risk assessments of HCM patients.

In previous studies, resting MBF did not statistically significantly differ between the healthy volunteers and the HCM patients[4]; although, no consensus for optimally measuring this parameter has yet been established.[16] $Slope_{max}$ was derived from the time–intensity curves of myocardial MRI perfusion studies. This parameter can be easily calculated in routine clinical practice[15] from time–intensity curves and reflects myocardial perfusion. $Slope_{max}$ can be normalized to the LV cavity to avoid variations based on arterial inflow. Theoretically, diseased myocardium should exhibit a relatively longer wash-in time due to the destruction of coronary microcirculation, thus decreasing the $slope_{max}$.[17] In concordance with this, myocardium in HCM patients in the present study exhibited statistically significantly lower $slope_{max}$ as compared to healthy myocardium in normal volunteers. A previous MRI study[18] showed perfusion defects could be observed in HCM patients, but they did not quantify the finding. In the present study, similar differences in $slope_{max}$ were observed between hypertrophic and non-hypertrophic myocardial segments in HCM patients. Hypertrophic myocardium exhibited a statistically significantly less physiological thickening relative to that of the control group, a finding consistent with the proposed pathophysiological mechanism of HCM noted above. It is also consistent to the results of Camici et al. reporting microvascular dysfunction in both hypertrophic and non-hypertrophic segments using PET.[19]

$Slope_{max}$ values were also decreased in myocardial segments with more severe hypertrophy, which is in agreement with hyperaemia MBF (hMBF) data using first-pass MRI and the other methods.[4] $Slope_{max}$ and the degree of myocardial thickening were also negatively correlated with EDTH. These results together imply a strong correlation between the extent of myocardial hypertrophy and coronary microvascular dysfunction.[20] These findings may relate to a reduction in microvascular density with increasing LV mass.[21] Although in the present study, the degree of thickening in segments with mild and moderate hypertrophy did not statistically significantly differ. Nonetheless, the $slope_{max}$ appears to more sensitively detect abnormalities associated with HCM than do measurements of myocardial thickening, presumably related to the early detection of microvascular dysfunction.

Late gadolinium enhancement in CMR is likewise a sensitive, specific, and reproducible measure, which demonstrates excellent agreement with SPECT and PET in the evaluation of myocardial perfusion and metabolism.[22–24] The presence of LGE reflects myocardial fibrosis. Typical findings in HCM include patchy, multifocal enhancement of hypertrophic myocardial segments. In this study, the $slope_{max}$ of hypertrophic segments with LGE was statistically significantly less than that of hypertrophic segments without LGE, suggesting that myocardial perfusion in LGE segments was more severely impaired. The mechanism for myocardial fibrosis in HCM is not clear but could relate to microvascular dysfunction. Previous studies[25–27] have reported myocardial fibrosis to be the result of myocardial ischaemia, finding that regions of microvascular dysfunction corresponded to regions where microvascular intramural proliferation was present histopathologically. Other studies[26,28,29] have shown myocardial fibrosis to be related to the presence of increased intercellular connective tissue. In the present work, hypertrophic segments with LGE demonstrated greater EDTH and less thickening compared to segments without LGE. In total, these findings suggest that segments with LGE likely exhibit myocardial fibrosis, possibly as a result of microvascular dysfunction. They are in agreement with the results of Sotgia et al., who investigated relationship between hMBF using PET and LGE using MRI.[30]

The degree of coronary microvascular dysfunction is a strong, independent predictor of morbidity and mortality in HCM.[2] Severe microvascular dysfunction is an early predictor of clinical outcome even in HCM patients with mild or no symptoms. First-pass myocardial MR perfusion can detect regional microvascular dysfunction reliably, in combination with cine and/or delayed contrast-enhanced CMR. By using a multi-parametric approach assessing EDTH, myocardial thickening, LV function, and myocardial perfusion, the severity of microvascular dysfunction can be determined. In the present study, CMR perfusion studies were performed with the patients at rest and demonstrated differences in perfusion between HCM patients and normal volunteers. This approach, which does not rely on stress imaging, avoids risks associated with vasodilator administration and diminishes the risk of nephrogenic systemic fibrosis for patients with severe renal dysfunction as repeated gadolinium chelate administrations are unnecessary. Comparison of the sensitivities of rest and stress perfusion CMR represents an interesting topic for future investigation.

One limitation of this study is the relatively small sample size (22 patients). This may account for the lack of statistically significant differences observed between segments with moderate and severe hypertrophy. Although the $slope_{max}$ and the degree of thickening inversely correlated with EDTH, both correlation coefficients were relatively low ($r = -0.264$ and $r = -0.312$), a fact that may again relate to

the small sample size. Long-term clinical follow-up was also not available for the HCM patients.

In conclusion, the $slope_{max}$ of time–intensity curves from first-pass CMR perfusion studies is reduced in patients with HCM, preferentially so in hypertrophic myocardium, and decreases with the severity of segmental hypertrophy. This likely relates to the presence of microvascular dysfunction. Assessment of this parameter may thus aid in assessing the risk of myocardial ischaemia and myocardial fibrosis in HCM patients.

References

1. Elliott P, McKenna WJ. Hypertrophic cardiomyopathy. *Lancet* 2004;**363**:1882–91.
2. Cecchi F, Olivotto I, Gistri R, et al. Coronary microvascular dysfunction and prognosis in hypertrophic cardiomyopathy. *N Engl J Med* 2003;**349**:1027–35.
3. Moon JC, McKenna WJ, McCrohon JA, et al. Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. *J Am Coll Cardiol* 2003;**41**:1561–7.
4. Petersen SE, Jerosch-Herold M, Hudsmith LE, et al. Evidence for microvascular dysfunction in hypertrophic cardiomyopathy: new insights from multiparametric magnetic resonance imaging. *Circulation* 2007; **115**:2418–25.
5. Desai MY, Dhillon A, To ACY. Cardiac magnetic resonance in hypertrophic cardiomyopathy. *Curr Cardiol Rep* 2010;**13**:67–76.
6. O'Hanlona R, Teo K, Bucciarelli-Ducci C, et al. Perfusion CMR and SPECT in hypertrophic cardiomyopathy. *Int J Cardiol* 2008;**129**:e27–9.
7. Wilke N, Jerosch-Herold M, Wang Y, et al. Myocardial perfusion reserve: assessment with multisection, quantitative, first-pass MR imaging. *Radiology* 1997;**204**:373–84.
8. Bauner KU, Reiser MF, Huber AM. Low dose gadobenate dimeglumine for imaging of chronic myocardial infarction in comparison with standard dose gadopentetate dimeglumine. *Invest Radiol* 2009;**44**:95–104.
9. Cherryman GR, Pirovano G, Kirchin MA. Gadobenate dimeglumine in MRI of acute myocardial infarction. *Invest Radiol* 2002;**37**:135–45.
10. Balci NC, Inan N, Anik Y, et al. Low-dose gadobenate dimeglumine versus standard-dose gadopentate dimeglumine for delayed contrast-enhanced cardiac magnetic resonance imaging. *Acad Radiol* 2006;**13**:833–9.
11. Hundley WG, Bluemke DA, Finn JP, et al. ACCF/ACR/AHA/NASCI/SCMR 2010 expert consensus document on cardiovascular magnetic resonance. *J Am Coll Cardiol* 2010;**55**:2614–62.
12. Spiewak M, Malek LA, Misko J, et al. Comparison of different quantification methods of late gadolinium enhancement in patients with hypertrophic cardiomyopathy. *Eur J Radiol* 2010;**74**:e149–53.
13. Ommen SR. Hypertrophic cardiomyopathy. *Curr Probl Cardiol* 2011;**36**:409–53.
14. Marian AJ. Pathogenesis of diverse clinical and pathological phenotypes in hypertrophic cardiomyopathy. *Lancet* 2000;**355**:58–60.
15. Jerosch-Herold Ml. Quantification of myocardial perfusion by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2010;**12**:57.
16. Jerosch-Herold M, Seethamraju RT, Swingen CM, et al. Analysis of myocardial perfusion MRI. *J Magn Reson Imaging* 2004;**19**:758–70.
17. Tian C, Xie J. Preliminary study of magnetic resonance first-pass myocardial perfusion imaging in hypertrophic cardiomyopathy. *Chin J Med Imaging Technol* 2003;**19**:170–1.
18. Melacini P, Corbetti F, Calore C, et al. Cardiovascular magnetic resonance signs of ischemia in hypertrophic cardiomyopathy. *Int J Cardiol* 2008;**128**:364–73.
19. Camici P, Chiriatti G, Lorenzoni R, et al. Coronary vasodilation is impaired in both hypertrophied and nonhypertrophied myocardium of patients with hypertrophic cardiomyopathy a study with nitrogen-13 ammonia and positron emission tomography. *JACC* 1991;**17**:879–86.
20. Knaapen P, Germans T, Camici PG, et al. Determinants of coronary microvascular dysfunction in symptomatic hypertrophic cardiomyopathy. *Am J Physiol Heart Circ Physiol* 2007;**294**:H986–93.
21. Krams R, Kofflard MJM, Duncker DJ, et al. Decreased coronary flow reserve in hypertrophic cardiomyopathy is related to remodeling of the coronary microcirculation. *Circulation* 1998;**97**:230–3.
22. Zhao S, Yan C, Yang M, et al. Identification of viable myocardium delay enhancement magnetic resonance imaging and 99Tcm-sestamibi or 18F-fluorodeoxyglucose single photon emission computed tomography. *Chin J Cardiol* 2006;**34**:1072–6.
23. Simonetti OP, Kim RJ, Fieno DS, et al. An improved MR imaging technique for the visualization of myocardial infarction. *Radiology* 2001; **218**:215–23.
24. Berman DS, Hachamovitch R, Shaw LJ, et al. Roles of nuclear cardiology, cardiac computed tomography, and cardiac magnetic resonance: assessment of patients with suspected coronary artery disease. *J Nucl Med* 2006;**47**:74–82.
25. Maron BJ, Wolfson JK, Epstein SE, et al. Intramural ("small vessel") coronary artery disease in hypertrophic cardiomyopathy. *JACC* 1986; **8**:545–57.
26. Choudhury L, Mahrholdt H, Wagner A, et al. Myocardial scarring in asymptomatic or mildly symptomatic patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002;**40**:2156–64.
27. Mahrholdt H. Delayed enhancement cardiovascular magnetic resonance assessment of non-ischaemic cardiomyopathies. *Eur Heart J* 2005;**26**:1461–74.
28. Shirani A, Pick R, Roberts WC, et al. Morphology and significance of the left ventricular collagen network in young patients with hypertrophic cardiomyopathy and sudden cardiac death. *JACC* 2000;**35**:36–44.
29. Moon JCC, Reed E, Sheppard MN, et al. The histologic basis of late gadolinium enhancement cardiovascular magnetic resonance in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2004;**43**:2260–4.
30. Sotgia B, Sciagra R, Olivotto I, et al. Spatial relationship between coronary microvascular dysfunction and delayed contrast enhancement in patients with hypertrophic cardiomyopathy. *J Nucl Med* 2008;**49**: 1090–6.