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

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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.

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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 $\geq$15 mm or $\geq$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 $\times$ 320 mm field of view (FOV), 224 $\times$ 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 $\times$ 270 mm FOV, 128 $\times$ 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 $\times$ 324 mm FOV, 192 $\times$ 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 $\geq$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).