Case Report

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Usefulness of MRI to Demonstrate the Mechanisms of Myocardial Ischemia in Hypertrophic Cardiomyopathy with Myocardial Bridge

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Key Words
Bridging · Coronary imaging · Hypertrophic cardiomyopathy · MRI · Myocardial ischemia

Abstract
We present a case of symptomatic primary hypertrophic cardiomyopathy (HCM) associated with myocardial bridging of the left anterior descending (LAD) artery and suspected ischemia that could be related either to LAD artery compression or to microvascular perfusion abnormalities. MRI demonstrated the morphological appearance of myocardial hypertrophy, and coronary MR angiography evidenced the myocardial bridge and its functional consequences with stress MR perfusion. In conclusion, as a non-invasive comprehensive imaging technique, MRI should be considered in identifying the mechanisms of myocardial ischemia in HCM with myocardial bridge.

Introduction

Primary hypertrophic cardiomyopathy (HCM) is characterized by left ventricular hypertrophy in the absence of any other cause of increased cardiac mass and is now linked to mutations in genes coding for myofibrillary proteins. Anginal symptoms and signs of ischemia frequently occur in those patients without detectable lesions of the major epicardial arteries, suggesting that ischemia results in abnormalities in the coronary microcirculation. However, HCM is also frequently associated with myocardial bridging. Thus, to choose the appropriate therapy, it is of great importance to precisely identify the mechanism of the ischemia that can be due either to microvascular perfusion abnormalities or to extrinsic coronary compression.

Case Report

A 19-year-old woman with known HCM was referred to our institution with a recent history of chest pain and syncope. Her mother was followed up for HCM that was related to a R717Q myosin heavy chain mutation. Echocardiography was performed as a first-choice imaging technique, showing a moderate hypertrophic myocardium with a maximal outflow gradient of 47 mm Hg that could not explain the symptoms by itself. X-ray coronary angiography was then performed and demonstrated myocardial bridging in the middle segment of the left anterior descending (LAD) coronary artery during systole, with systolic coronary compression, without significant residual diastolic compression, and without the presence of any other lesion (fig. 1a).

Cardiac MRI was then performed on a 1.5-tesla MR imager (Philips, Best, The Netherlands) with patients in the supine position. ECG-triggered cine-MRI sequences were first acquired in multiple orientations. Mid-diastolic and end-systolic coronary MR angiograms were then consecutively acquired during free breathing, using a navigator-echo, ECG-gated, radial, three-di-

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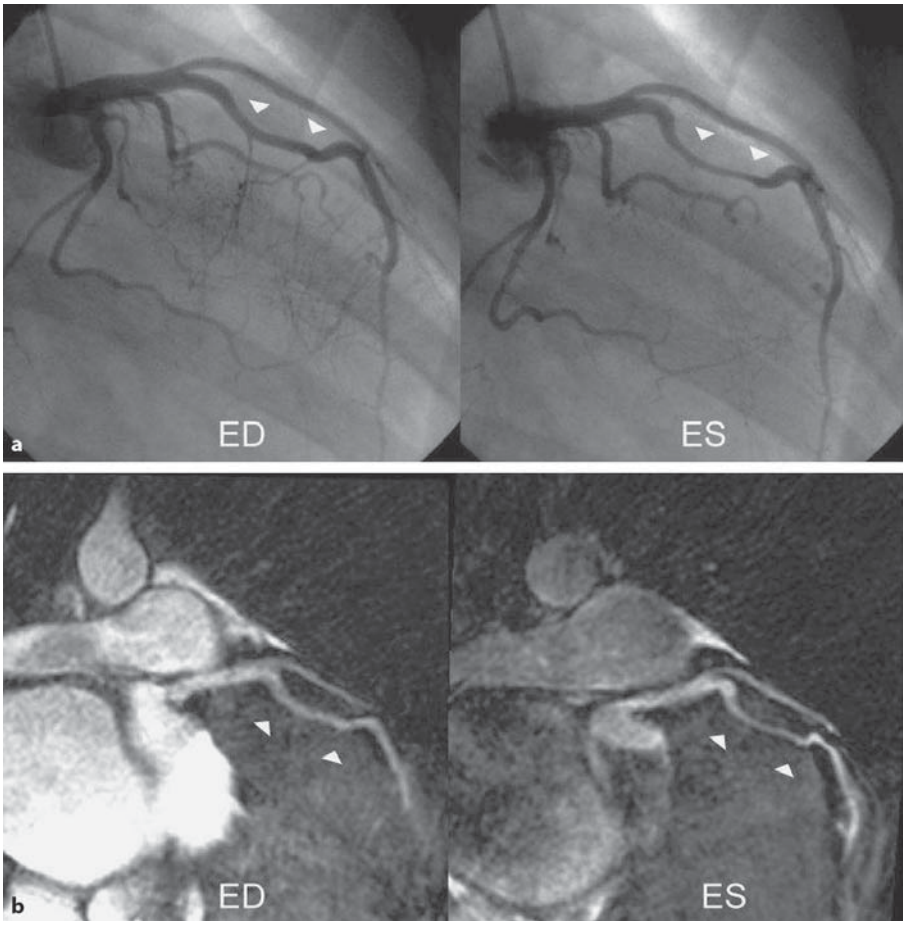

Fig. 1. a Coronary X-ray angiogram in right anterior oblique view of the LAD artery showing the course of the middle segment of the artery entrapped within the myocardium (arrows) at the end-diastolic and the end-systolic phase during the cardiac cycle. Note the narrowing of the artery at end-systolic phase. **b** Corresponding right anterior oblique view of the LAD artery on the coronary MR angiogram allowing to identify the muscular bridge, the course of the middle segment (arrows) and the variation in diameter of the vessel between end-diastolic and end-systolic phases.

mensional, balanced turbo field echo sequence [1]. First-pass MR perfusion imaging was also performed at three short-axis, basal, mid-ventricular, and apical left ventricular (LV) levels. A single-shot, segmented, hybrid echo planar imaging sequence was applied with the following parameters: TR/TE, 8.5/3.1 ms; flip angle, 30°; thickness, 8 mm, and in-plane resolution of 1.9 × 2.2 mm^2. First-pass images were acquired during bolus injection of gadolinium (Dotarem®: 0.1 mmol/kg at a flow rate of 6 ml/s; Guerbet, Aulnay-sous-Bois, France). Perfusion images were first acquired during pharmacologic stress (dipyridamole, 0.56 mg/kg). After stress imaging, reversal of the pharmacologic vasodilatation was achieved with aminophylline injection. Perfusion imaging was then obtained at rest (0.1 mmol/kg) 15 min later, after delayed enhanced MR (DE-MR) imaging using an inversion-recovery, three-dimensional, segmented gradient echo sequence, and with optimized inversion time to null normal myocardium signal.

Cine MR imaging confirmed LV hypertrophy with segments of normal end-diastolic thickness in the lateral wall (fig. 2). LV mass was 167 g (115 g/m^2) and LV ejection fraction was normal (69%). Coronary MR angiography allowed direct visualization of the myocardial bridge encompassing the middle segment of the LAD artery, but also determined the systolic narrowing of the LAD artery diameter compared to its normal diastolic diameter, closely matching the end-systolic and -diastolic diameters observed on X-ray coronary angiograms (fig. 1). Perfusion MR imaging under pharmacologic stress demonstrated a circumferential subendocardial hyposignal, with an unusual delayed wash-in of the contrast media in the subendocardium and progressive centripetal signal increase from the epicardium toward the endocardium over time (fig. 3). Hypoperfusion was not predominantly distributed to the LAD-depend segments and therefore could not be related to the extrinsic LAD compression (fig. 4). Rest MR perfusion images were interpreted as normal. DE-MR images showed patchy areas of intramyocardial hyperenhancement in hypertrophic segments without any specific distribution (fig. 5). Since added contribution of bridging to myocardial perfusion abnormalities was very unlikely, no surgical procedure was undertaken and medical treatment was prescribed.

Discussion

To the best of our knowledge, this is the first reported case of an HCM patient with myocardial bridge and suspected myocardial ischemia, indicating that comprehen-

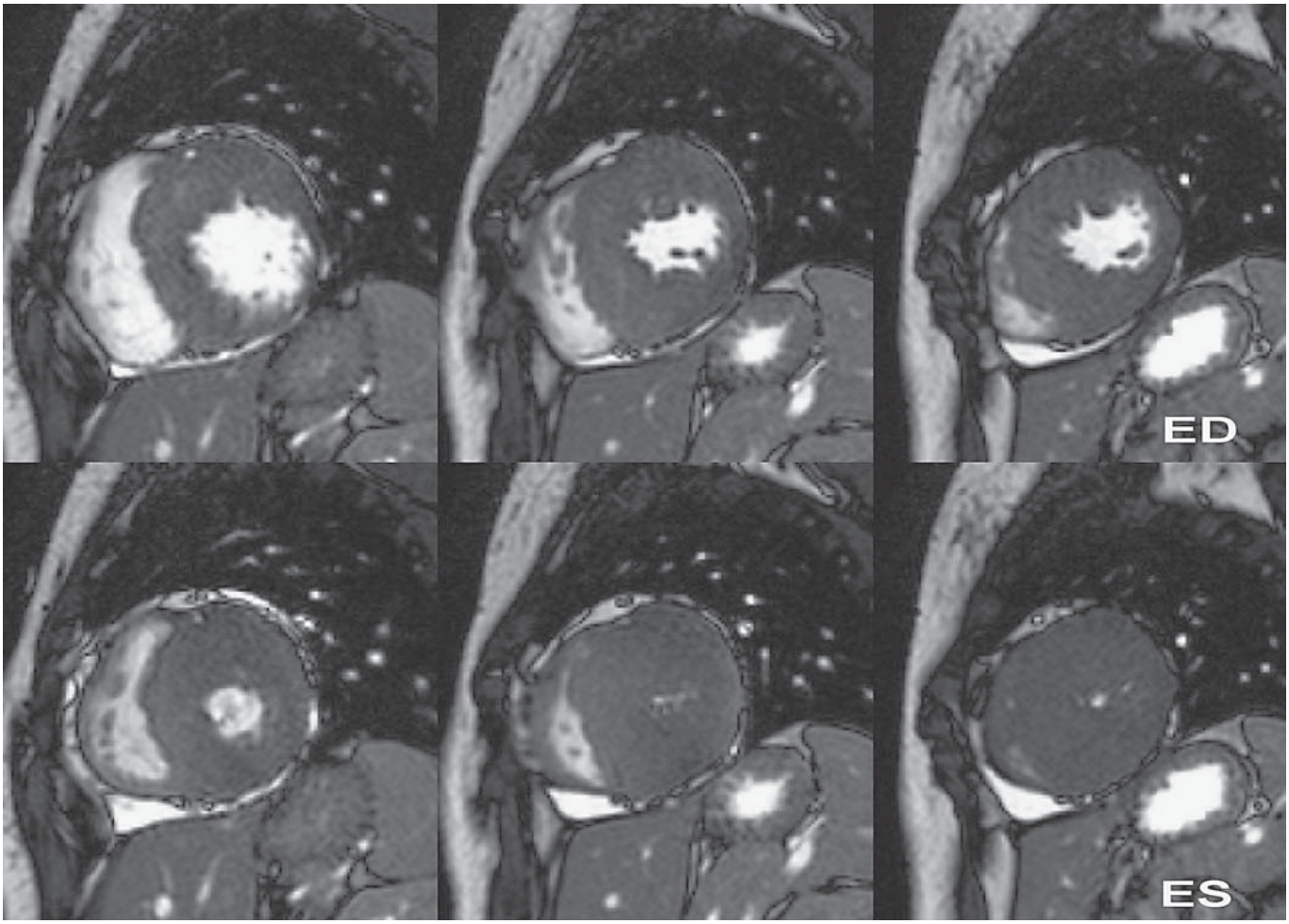

Fig. 2. Cine MRI in short-axis views at three levels from base to apex, showing LV hypertrophy and wall thickening from end-diastole to end-systole sparing lateral segments of normal end-diastolic thickness.

sive cardiac MRI may play a key role in identifying the mechanism of ischemia that could be related either to LAD compression or to microvascular perfusion abnormalities. MRI is an established reference method to accurately determine hypertrophic myocardium distribution and its functional consequences, e.g. outflow tract obstruction and mitral systolic anterior motion. It is also the most accurate clinically available method for assessing LV mass and progression over time because of its three-dimensional nature and excellent interstudy reproducibility [2]. The unique capability of post-gadolinium DE-MR imaging allowed identification of patchy hyperenhancement in hypertrophied regions related to myocardial fibrosis, predominantly involving the middle third of the ventricular wall, not corresponding to any particular epicardial coronary artery distribution and sparing the subendocardium, both conditions allowing differentiation from post-ischemic lesions [3]. Kim et al. [4] discussed that hyperenhanced tissue on gadolinium-enhanced images is unlikely to represent replacement scarring in HCM since different types of fibrosis may occur in the course of the disease. However, its finding remains of particular clinical interest since this abnormal pattern is linked to the risk of sudden death [3].

Coronary MR angiography successfully identified the end-systolic narrowing of the LAD artery due to the myocardial bridge but without residual diastolic compression of the coronary vessel, that closely matched X-ray coronary angiography findings. As only 15% of coronary flow occurs during systole, bridging may be postulated to cause myocardial ischemia in the presence of persisting diastolic compression of the coronary vessel, as shown by

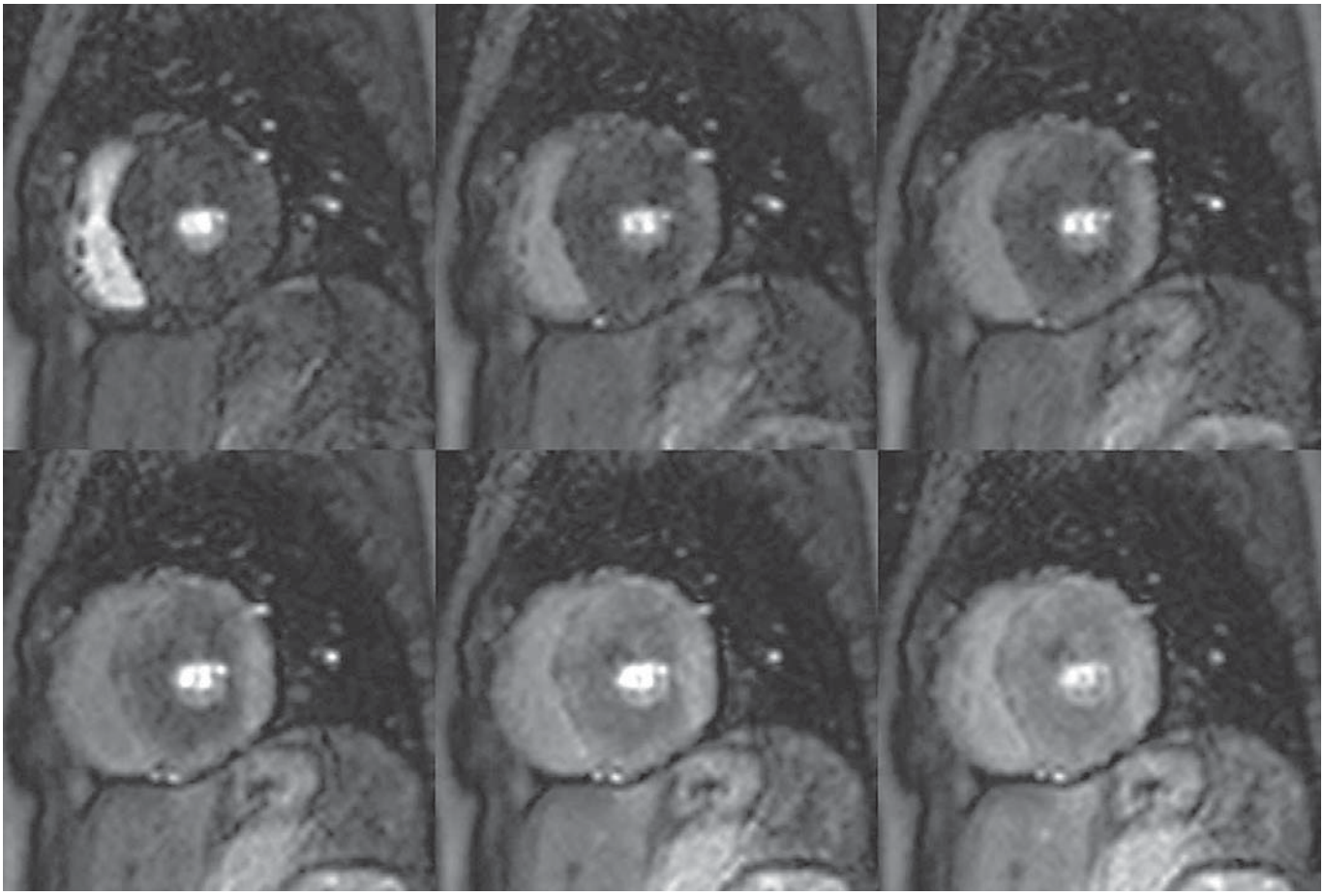

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Fig. 3. First-pass, perfusion image sequence at the mid-ventricular short-axis level during gadolinium bolus injection (0.1 mmol/kg; 6 ml/s flow rate) and dipyridamole stress showing a circumferential subendocardial hyposignal and delayed wash-in of the contrast media with a gradient from epicardium to endocardium. A progressive centripetal signal increase is noted over time corresponding to the delayed arrival of contrast media in the extracellular space.

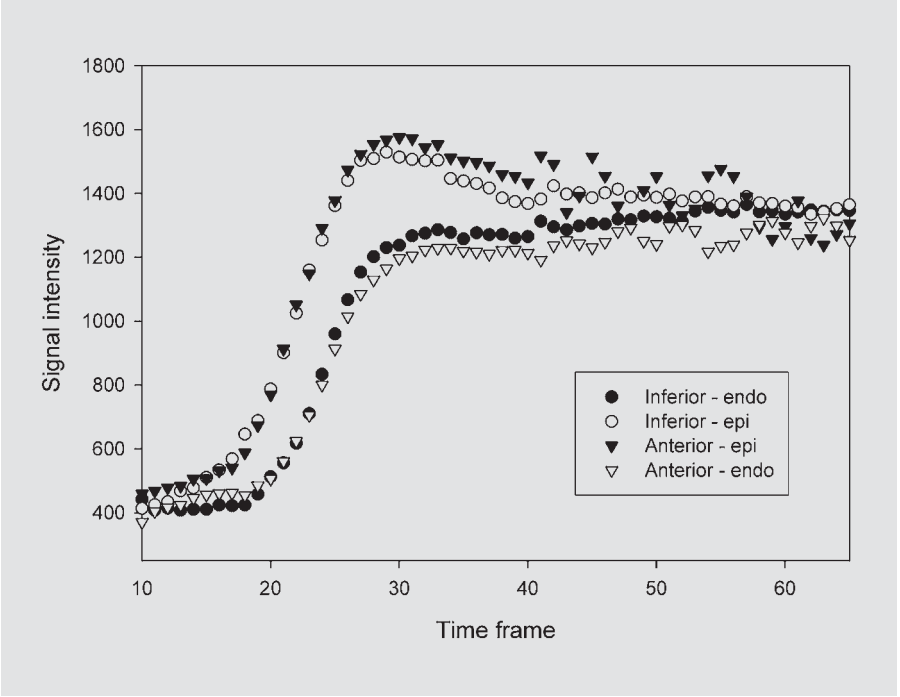

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Fig. 4. Signal intensity-time curves in selected epicardial and endocardial anterior (LAD-dependent) and posterior (right-coronary-dependent) regions of interest during dipyridamole stress, first-pass, perfusion MR imaging in the reported case. No difference in signal intensity curves is observed in both epicardial and endocardial regions of interest between the two anterior and posterior segments. A delayed wash-in of gadolinium is clearly demonstrated in subendocardial regions compared to subepicardial ones.

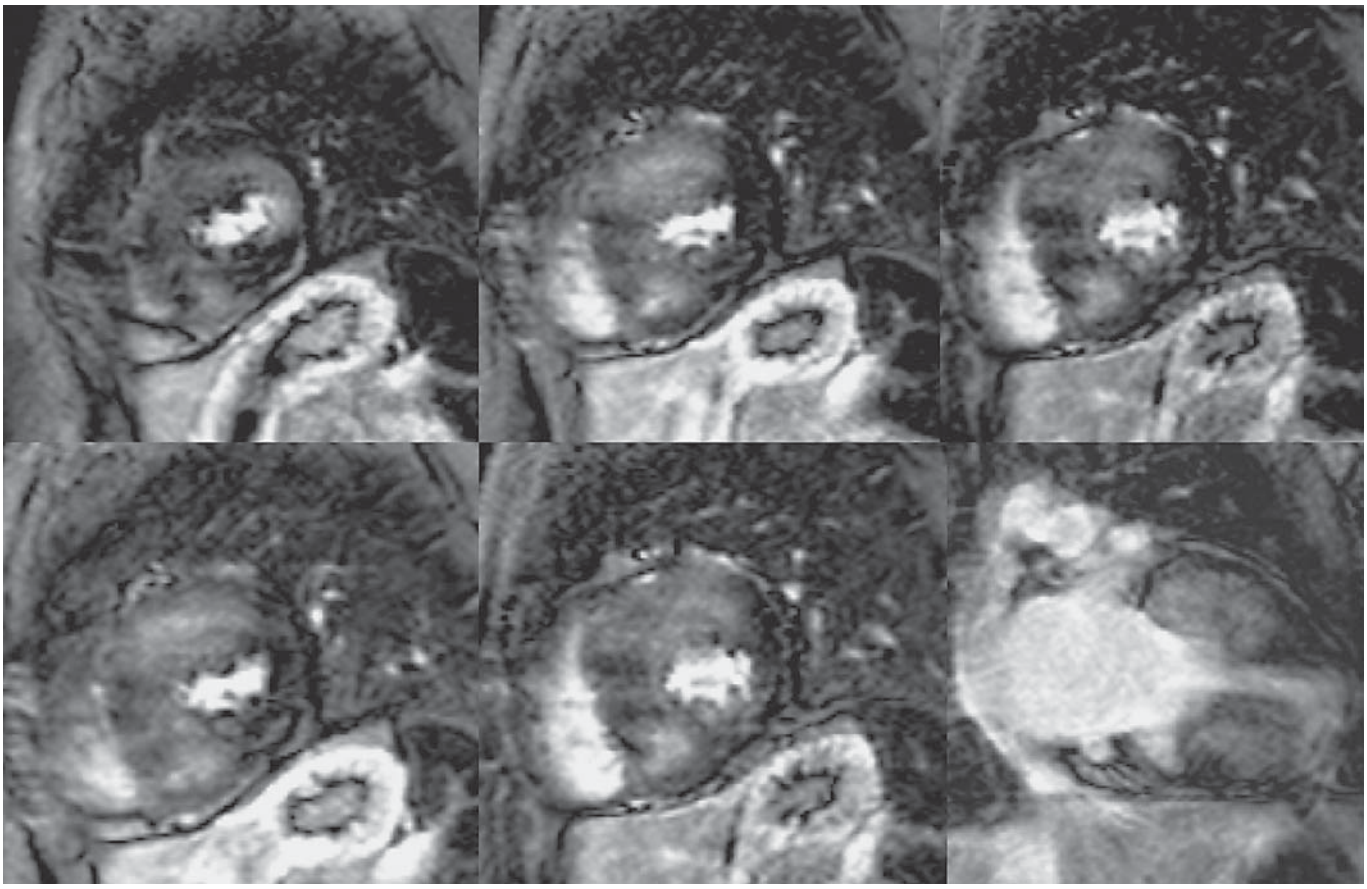

Fig. 5. DE-MR three-dimensional gradient echo sequence in short-axis view showing the patchy hyperenhanced regions located in hypertrophic segments.

Yetman et al. [5]. However, using X-ray coronary angiography, no study has been able to demonstrate that bridging may induce critical stenosis during diastole, and it has been suggested that alternative, refined methods, e.g. intracoronary ultrasound or perfusion imaging, may be required to identify the functional significance of bridging [6, 7]. X-ray coronary angiography, presently the gold standard for the diagnosis of a myocardial bridge, does not provide information on the functional impact at myocardial level [8]. The same limitation would remain if multidetector CT had been used to explore the coronary tree.

First-pass MR perfusion imaging performed at rest and under pharmacological stress can be used to detect impaired perfusion reserve in patients with coronary artery disease [9, 10]. More recently, first-pass MR imaging with pharmacologic stress was able to demonstrate a reduction in the first-pass reserve index in HCM patients [11]. Furthermore, segmental perfusion abnormalities were correlated with LV wall thickness. These findings were concordant with ^{201}Tl SPECT or ^{13}N-ammonia PET studies with proven reversible stress perfusion abnormalities involving predominantly subendocardial layers [12, 13]. In our case, we found not only a reversible circumferential stress hypoperfusion predominantly in subendocardial layers but also a specific pattern of transient delayed wash-in during the first pass of the contrast media with a progressive centripetal signal increase over time. To our knowledge, this dynamic and transient enhancement pattern has not been described in HCM patients previously. Static or dynamic scintigraphic acquisitions with a 5- to 10-second sampling rate at best lack also the requested temporal resolution to demonstrate this transient delayed wash-in pattern. Sipola et al. [11] used an inversion recovery perfusion imaging protocol with a relative low temporal resolution of 3–4 s. From a pathophysiological point of view, signs of ischemia that occur in HCM patients without detectable lesion of epicardial

arteries are reported to be the consequence of functional and/or structural abnormalities in the coronary microcirculation. Indeed, not only the extravascular compressive forces and particularly wall stress in the subendocardium may play a significant role in the occurrence of ischemic signs and the pattern we described, but also a decrease in capillary density and arteriolar remodeling with an abnormally thick wall are suspected to explain the impaired coronary reserve [14]. Ultimately, repeated episodes of exercise-induced ischemia may lead to fibrosis via the stimulation of collagen synthesis and explain DE-MR imaging findings [15].

Clinically, myocardial bridging with compression of epicardial vessels occurs in 30–50% of adults with HCM [16]. The role of myocardial bridging in ischemia and sudden death in patients with HCM remains controversial [17], but a poorer outcome of HCM combined with bridging has been outlined [18]. In case of clinical signs of both HCM and myocardial bridging, it seems of importance to determine the respective contribution of HCM and myocardial bridging in myocardial ischemia, since specific therapeutic options are currently proposed to treat myocardial bridging. Surgical myotomy or intracoronary stent implantation can be discussed to prevent external compression of the bridged coronary artery segment [8, 19]. For symptomatic HCM without myocardial bridging, medical treatment remains the first-line therapy, but septal ablation or myectomy have also been proposed [20].

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