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## Multimodality imaging in apical hypertrophic cardiomyopathy

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### Abstract

Apical hypertrophic cardiomyopathy (AHCM) is a relatively rare morphologic variant of HCM in which the hypertrophy of myocardium is localized to the left ventricular apex. Symptoms of AHCM might vary from none to others mimic coronary artery disease including acute coronary syndrome, thus resulting in inappropriate hospitalization. Transthoracic echocardiography is the first-line imaging technique for the diagnosis of hypertrophic cardiomyopathies. However, when the hypertrophy of the myocardium is localized in the ventricular apex might results in missed diagnosis. Aim of this paper is to review the different imaging techniques used for the diagnosis of AHCM and their role in the detection and comprehension of this uncommon disease.

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**Key words:** Apical hypertrophic cardiomyopathy; Imaging techniques; Cardiac magnetic resonance; Transthoracic echocardiography; Multidetector computed tomography

**Core tip:** Apical hypertrophic cardiomyopathy (AHCM) is a relatively rare morphologic variant of HCM in which the hypertrophy of myocardium is localized to the left ventricular apex. Aim of this paper is to review the dif-

### INTRODUCTION

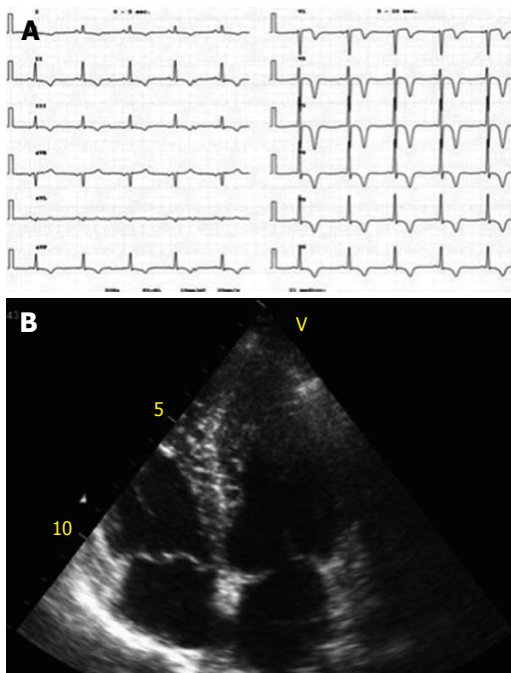
Hypertrophic cardiomyopathy (HCM) is a genetic disorder caused by mutations in one or more of the genes encoding protein components of the cardiac sarcomere and transmitted with an autosomal dominant trait and variable penetrance<sup>[1,2]</sup>. The variability of these mutations leads to different morphological features of the pathology and influences patient prognosis<sup>[3,4]</sup>.

Apical HCM (AHCM) is a relatively rare morphologic variant of HCM in which the hypertrophy of the myocardium is mainly localized to the left ventricular (LV) apex without the typical septal predominance, which characterize hypertrophic obstructive cardiomyopathy. A sarcomere protein gene defects have been found to be present from 13% to 30% of these patients<sup>[5]</sup>. It was first described in Japanese patients with precordial deep T wave inversions (referred to as giant T wave inversions) in 1976<sup>[6,7]</sup>. This condition is frequent in Asian population accounting for almost 25% of Japanese patients with HCM while its prevalence dramatically decrease in Caucasian patients to 1%-3%<sup>[8-10]</sup>. Male gender is the most frequently affected in the Japanese population but this gender difference has not been as relevant outside Japan<sup>[11]</sup>. Differences between the "pure" Japanese form of AHCM (hypertrophy of only the apical segments) and the non-Japanese form are reported. AHCM in Caucasian patients presents hypertrophy extended to the middle

**Table 1** Comparison of different imaging techniques

	Echocardiography	SPECT	Angiography	MDCT	CMR
LV morphology (dimensions, wall thickness)	++	-	+	++	+++
Global and regional LV function	++	+	+	++	+++
LV filling pressure	++	+	+++	+	++
Radiation	-	+	+	+	-
Ischemia/CAD	+	++	+++	++	++
Tissue characterisation	+	-	-	-	+++
Cost	-	+++	+++	++	++

SPECT: Single photon emission computed tomography; MDCT: Multidetector computed tomography; CMR: Cardiovascular magnetic resonance; LV: Left ventricular; CAD: Coronary artery disease.



**Figure 1** On transthoracic echocardiography, apical hypertrophic cardiomyopathy is defined as an absolute apical thickness of more than 15 mm with a ratio of apical to basal left ventricular wall thickness of more than 1.3. A: 12-lead electrocardiogram with increased in QRS voltage and deep T-wave inversion in the precordial leads; B: Transthoracic echocardiography 4-chambers view showing asymmetrical left ventricular apical thickening with a spade shaped left ventricle configuration.

left ventricle's segment segments ("mixed form"), with a worsened prognosis. These findings suggest a variability in the phenotypic expression of AHCM between countries and races with a possible additional role of environmental factors<sup>[12,13]</sup>.

AHCM has a relatively benign prognosis in terms of cardiovascular mortality ranging around 0.1% in "pure" forms. However, one-third of the patients may experience unfavourable clinical events and life treating complications: diastolic dysfunction, myocardial infarction, left atrial enlargement with subsequent atrial fibrillation, apical aneurysm and thrombi with ventricular arrhythmias<sup>[10,12]</sup>. Moreover, progression into apical aneurysm or mid-ventricular obstruction is a variant and unfavourable feature of the disease. Symptoms might vary from none to others including chest pain in absence of angiographi-

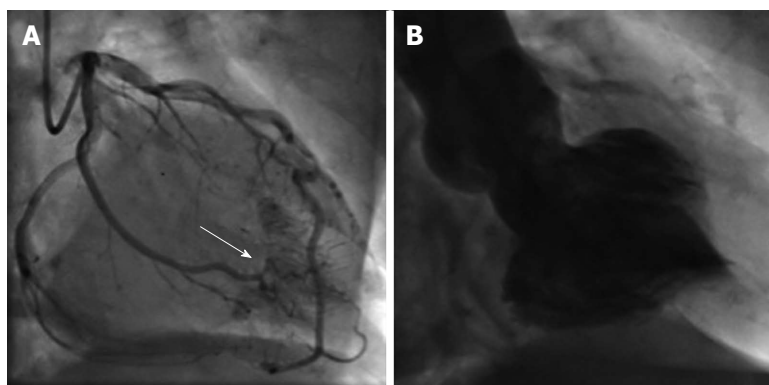
cally proven coronary stenosis, palpitations, dyspnea, fatigue or syncope<sup>[14]</sup>. ECG pattern found in up to 90% of cases, include giant negative T waves at rest with transient normalization on exertion. Transthoracic echocardiography is currently the standard diagnostic tool for hypertrophic cardiomyopathies, however its diagnostic accuracy for identification of hypertrophy confined to the LV apex is limited.

Aim of this paper is to briefly review the different imaging techniques in the diagnosis of AHCM and their potential role in expanding our knowledge of this uncommon disease (Table 1).

## ECHOCARDIOGRAPHY

Transthoracic echocardiography (TTE) is the first line imaging exam in patient with suspected AHCM because of its widespread availability and low-cost. On TTE, AHCM is defined as an absolute apical thickness of more than 15 mm with a ratio of apical to basal LV wall thickness of more than 1.3 (Figure 1). According to patterns of hypertrophy, two morphologically distinct phenotypes have been described: pure AHCM where the hypertrophy is limited to the apical segments and mixed AHCM with hypertrophy extending to the mid-ventricular level, sparing the basal segments<sup>[15]</sup>. Morphological subtypes have been found to be predictors of different prognosis and clinical manifestations<sup>[16]</sup>. Tissue Doppler technique enables to document a lowered coronary flow reserve capacity of penetrating intramyocardial coronary arteries<sup>[17]</sup>. However, because of technical artefacts and variability of imaging quality, TTE might results in poor detection of endocardial border thus resulting in misleading diagnosis<sup>[18]</sup>. Patients with AHCM might develop apical aneurysms and clots mimicking other conditions such as cardiac tumor, isolated ventricular non-compaction, endomyocardial fibrosis, *etc.* The use of microbubbles contrast agent may improve diagnostic sensitivity<sup>[19-23]</sup>.

Newer Doppler-based techniques have been successfully applied in the diagnosis of AHCM. Reddy *et al.*<sup>[24]</sup> described paradoxical apical longitudinal strain (systolic lengthening) in two patients with AHCM despite an apparently normal apical wall motion on conventional TTE. Abecasis *et al.*<sup>[25]</sup> using velocity vector imaging tissue characterization study found abnormal regional velocities and



**Figure 2 Angiography pictures.** A: Coronary angiography showing normal epicardial coronary arteries. Please note the presence of multiple coronary artery-left ventricular microfistulae (white arrow); B: Left ventricular angiography showing the characteristic diastolic “ace-of-spade” sign.

deformation parameters, particularly concerning base to apex longitudinal strain gradient, that could be related to the abnormal tissue hypertrophy extending beyond the more evident apical hypertrophic segments.

Multipane transoesophageal echocardiography enables a correct visualization and sizing of ventricular segments and has been successfully applied in the diagnosis of AHCM<sup>[26]</sup>.

## SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

Radionuclide scanning has also been used in diagnosis of AHCM. Reports of stress myocardial perfusion images in patients with AHCM have ranged from normal perfusion to reversible and fixed apical perfusion defects, often in the presence of normal epicardial coronary arteries<sup>[27]</sup>. The unbalanced wall thickness-to-vascular supply ratio leads to a relative apical ischemia<sup>[28,29]</sup>. Myocardial ischemic chest pain in the absence of coronary artery disease (CAD) has been related to limited coronary flow reserve in patients with asymmetric septal an apical hypertrophy<sup>[29-32]</sup>. Morishita *et al*<sup>[33]</sup> have also described increased uptake of Tc-99 m tetrofosmin in the apical segment on resting Single Photon Emission Computed Tomography (SPECT) polar maps in a subgroup of patients with AHCM. AHCM increased apical tracer uptake on resting Tl-201 planar and SPECT imaging has been previously reported<sup>[34]</sup>. Ward *et al*<sup>[35]</sup> showed a newly “Solar Polar” map pattern at rest. This “Solar Polar” map pattern on resting Tl-201 volume-weighted polar maps, sees an intensely bright spot of counts in the apical segment surrounded by a circumferential ring of decreasing counts. This study is the first describing the typical findings on dual-isotope rest and stress SPECT perfusion images and volume-weighted polar maps in non-Japanese patients with AHCM. Three different patterns characteristic of AHCM were identified<sup>[36]</sup>: an increased apical tracer uptake, a spade-like configuration of the LV chamber and the “Solar map” in 75% of patients; however no difference in apical thickness and magnitude of T-wave negativity between patients with normal SPECT and typical

pattern were observed. Interstitial fibrosis that prevented the increased apical tracer uptake is the possible explanation for a normal SPECT study in patients with AHCM.

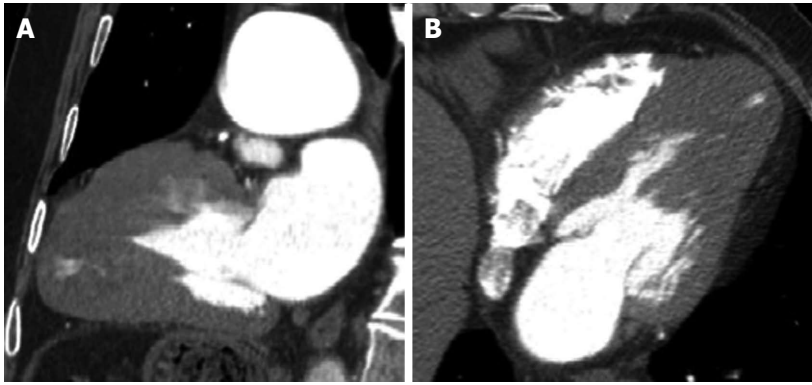
## ANGIOGRAPHY

ECG changes and symptoms associated with AHCM often mimic acute coronary syndromes. Moreover elevated troponine serum levels reported in patients with AHCM and chest pain usually encourage physicians to perform invasive testing. Coronary angiography allows to exclude significant epicardial coronary lesions and enables detection of the associated congenital coronary artery anomalies, myocardial bridge or multiple coronary-LV fistulae<sup>[37]</sup>. Evaluation of the LV cavity can show the characteristic spade-like configuration of the left ventricle in end-diastole, with obliteration of the apical cavity in end-systole due to the vigour contraction of the hypertrophied myocardium<sup>[7]</sup> (Figure 2). Caucasian patients tend to have less localized involvement of the distal apex resulting in a lower frequency of the pathognomonic sign of “ace-of-spade” on the left ventriculography<sup>[13]</sup>.

## MULTIDETECTOR COMPUTED TOMOGRAPHY

Coronary multidetector computed tomography (MDCT) is an high sensitive (91%-99%) and specific (74%-96%) technique in detecting significant coronary stenosis<sup>[38-40]</sup>. Major international guidelines currently indicate coronary MDCT for patients at a low to intermediate risk of CAD<sup>[41]</sup> and his adoption in the emergency room might facilitate early triage of patients presenting chest pain<sup>[42-44]</sup>.

MDCT has also emerged as a novel technique for evaluating cardiac morphology and function. Initial concern with MDCT examination with radiation exposure have been overcome by novel technologies using dose-saving strategies<sup>[45,46]</sup>. Due to its high spatial resolution, MDCT can offer cardiac anatomical and functional information and a high quality non-invasive coronary evaluation<sup>[47-50]</sup>. It also enables accurate delineation of the apical endocardial border and dynamic evaluations of myocar-



**Figure 3** Multidetector computed tomography imaging: Long axis view (A) and axial scans at the level of the left ventricle (B) showing apical hypertrophy with cavity obliteration and a sequestered small left ventricle cavity.

dial thickness, global and regional LV functions<sup>[51]</sup>. Multi-planar reconstructions along major cardiac axis allow to measure myocardial thickness on short-axis view in the end-diastolic phase while the apex can be evaluated in long axis planes (Figure 3). Knickelbine *et al.*<sup>[52]</sup> have found nonatherosclerotic-related cardiovascular abnormalities judged to be of potential clinical relevance in 4.4% of 4543 patients with suspected atherosclerotic CAD undergoing to 64-slice MDCT. In 50 of these patients (1.1%) the abnormality was previously unrecognized. The most common abnormalities were: congenital coronary artery anomalies (38%), ascending aortic aneurysms > 45 mm (22%), hypertrophic cardiomyopathy with apical LV wall thickening (14%), valvular heart diseases (8%), congenital heart diseases including ventricular septal defect (6%), pulmonary embolus (6%), LV noncompaction, left atrial myxoma, and LV apical aneurysm (2%). Chen *et al.*<sup>[53]</sup> have performed MDCT in 14 patients with known diagnosis of AHCM. Left ventricle shapes reconstructions of MDCT were similar to angiography, with “ace-of-spades” configurations, apical sequestrations and apical aneurysm. Furthermore, MDCT was able to detect two cases of significant coronary stenosis and 7 patients with myocardial bridges.

## CARDIOVASCULAR MAGNETIC RESONANCE

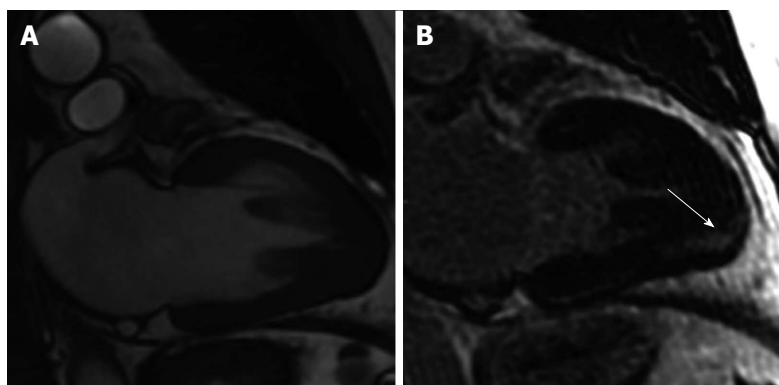
In the last few years cardiovascular magnetic resonance (CMR) has emerged as a useful and accurate imaging technique for diagnosis of HCM. Both European and American Cardiology Society indicated CMR as first choice exam or at least equivalent to other diagnostic methods in the approach of several cardiomyopathies, including HCM<sup>[54,55]</sup>.

The excellence of CMR in analyse anatomy and function has increased the sensitivity and specificity of the diagnosis of HCM<sup>[56]</sup>. A comparative study of TTE and CMR among HCM subjects demonstrated the greater accuracy of CMR identifying different patterns of hypertrophy. Among subjects with confined hypertrophy in anterolateral wall, echocardiography underestimates wall

thickness and poorly evaluates the apical segments in up to 40%<sup>[57-59]</sup>. AHCM may mimic other pathological conditions such as coronary artery disease, myocardial tumor, ventricular aneurysm, ventricular non-compaction or endomyocardial fibrosis and CMR can be useful in differential diagnosis. CMR provides a more accurate assessment of LV apical hypertrophy allowing detection of HCM related complications and wall motion abnormalities (Figure 4). Tsukamoto *et al.*<sup>[60]</sup> using CMR-tagging showed systolic outward motion of the LV apical wall in AHCM patients. LV apical aneurysms have been reported in up to 2% of all patients with HCM, with a rate of related adverse events of 10.5% per year, considerably higher with respect to HCM without aneurysm<sup>[61]</sup>. Notably, a higher incidence of apical aneurysms, ranging from 10% to 20%<sup>[62,63]</sup>, has been reported in AHCM. In a case series, Fattori *et al.*<sup>[64]</sup> showed that TTE was able to detect only 1 of the 4 cases of AHCM related apical aneurysms, suggesting the use of CMR in all patients affected by AHCM in order to confirm the diagnosis and to ascertain the presence of aneurysms. Indeed, the presence of an apical aneurysm, especially if associated with the detection of ventricular tachyarrhythmias, could support the decision to implant a cardioverter-defibrillator.

CMR appears to be more sensitive than other imaging techniques in detecting infarct areas and ischemia, identifying even subendocardial infarction with late gadolinium-enhanced (LGE)<sup>[65,66]</sup>. LGE-CMR has been used to visualize myocardial interstitial abnormalities in patients with different forms of cardiomyopathies, including non-ischemic forms<sup>[67,68]</sup>. LGE has been found to be present in a high proportion of patients with HCM and has been associated with a higher incidence of ventricular tachycarrythmias and risk of sudden death<sup>[69,70]</sup>. In patients with apical hypertrophic cardiomyopathy, the incidence of LGE seems to be less common with respect to other form of HCMP, but it is similarly associated to a worse prognosis. In the largest available series of AHCM patients imaged with magnetic resonance imaging, LGE was reported only in 40% of cases and limited to the hypertrophic apical segments<sup>[71]</sup>. However, others studies showed that LGE was not limited to the hypertrophic





**Figure 4 Cardiovascular magnetic resonance imaging.** Long axis view (A) of the left ventricle showing apical regional hypertrophy; long axis view 10 min after Gadolinium injection; B: An abnormal hyper-enhancement of the apical segment is visible (white arrow).

apical segments but also present in the midventricular and basal segments of interventricular septum, potential expression of myocardial damage preceding the abnormal hypertrophy. LGE-CMR should be applied for longitudinal follow-up studies to detect development and progression of AHCM related fibrotic tissue formations highlighting the subsets of patients associated with worse prognosis<sup>[72]</sup>.

## CONCLUSION

The correct diagnosis of AHCM is of major importance. Multimodality imaging is essential in increasing the detection of AHCM, yielding larger study populations. In particular, CMR showed an excellent accuracy in identifying the abnormal LV hypertrophy. With late gadolinium enhancement, CMR is able to *in vivo* detect abnormal myocardial structure allowing a more accurate risk stratification.

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