

# Late onset apical hypertrophic cardiomyopathy: a case report

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Received 4 May 2020; first decision 15 June 2020; accepted 18 November 2020

## Background

Apical hypertrophic cardiomyopathy provides diagnostic challenges through varying presentation, impaired visualization on echocardiography and dissent on diagnostic criteria. While hypertrophic cardiomyopathy in general requires an absolute wall thickness  $\geq 15$  mm, a threshold for relative apical hypertrophy (ratio 1.5) has been proposed.

## Case summary

We report the case of a 57-year-old man with newly arisen chest pain and slight T-wave inversions. Serial cardiac magnetic resonance imaging over 9 years documented the gradual evolvement of late-onset apical hypertrophy with apical fibrosis and strain abnormalities. Symptoms, electrocardiographic changes, and relative apical hypertrophy preceded the traditional imaging criteria of hypertrophic cardiomyopathy.

## Discussion

Relative apical hypertrophy can be an early manifestation of apical hypertrophic cardiomyopathy. Persistent cardiac signs and symptoms warrant a follow-up, as apical hypertrophic cardiomyopathy can evolve over time. Cardiac magnetic resonance imaging readily visualizes apical hypertrophic cardiomyopathy and associated changes in tissue composition and function.

## Keywords

Apical HCM • CMR • Strain • Parametric mapping • Case report

## Learning points

- Apical hypertrophic cardiomyopathy can develop gradually at a later age in a previously asymptomatic individual.
- Symptoms, T-wave inversions, and relative apical hypertrophy precede classical criteria for hypertrophic cardiomyopathy.
- Cardiac magnetic resonance readily distinguishes relative apical hypertrophy and apical hypertrophic cardiomyopathy from other causes of chest pain and visualizes accompanying alterations in function and tissue composition.

## Introduction

Apical left ventricular hypertrophy is a variant of hypertrophic cardiomyopathy (HCM) first described in 1976 with a predilection for

middle-aged men.<sup>1,2</sup> Because of technical limitations in the visualization of the apical endocardial border, mild forms of apical HCM can be missed by transthoracic echocardiography.<sup>3,4</sup> The condition is more commonly diagnosed in Asian compared to western

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Handling Editor: Belinda Grey

Peer-reviewers: Brian Halliday and Golnaz Houshmand

Compliance Editor: Carlos Minguito Carazo

Supplementary Material Editor: Vassilios Parisis Memtsas

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countries.<sup>5</sup> This might be partly attributable to lower awareness of the disease in western countries, as a comparative study using a consistent methodology and definitions found no relevant difference with an apical hypertrophy pattern in 13% of Japanese and 11% of European HCM patients.<sup>6</sup> Diagnostic criteria for apical HCM are evolving, with no consensus yet. While some groups have suggested an apical wall thickness of  $\geq 15$  mm together with a ratio of maximal apical to posterior wall thickness  $\geq 1.5$ , others have suggested relative apical hypertrophy, defined by an apical wall thickness exceeding basal wall thickness, as a sufficient diagnostic criterion for apical HCM.<sup>2,7,8</sup> The development and progression of 'classical' HCM is attributed to sarcomeric mutations and usually manifests in childhood or early adulthood.<sup>9–11</sup> With apical HCM, a later onset, better prognosis, and weaker genotype–phenotype correlation are observed.<sup>2,12,13</sup>

## Timeline

Timeline:	
2010 (age 57)	Patient presented with atypical chest pain and slight T-wave inversions in V5. Cardiac magnetic resonance (CMR) imaging: No ischaemia, left ventricular (LV) wall thickness apical 8 mm, posterior basal 7 mm (ratio 1.1)
2013	Anterolateral T-wave inversions. CMR: no ischaemia, LV wall thickness apical 11 mm, posterior basal 7 mm (ratio 1.6)
Late 2018	New dyspnoea New York Heart Association II, global T-wave inversions. Coronary artery disease excluded by catheter.
Early 2019	CMR: LV wall thickness apical 16 mm, posterior basal 9 mm (ratio 1.8), apical fibrosis, and strain abnormalities.

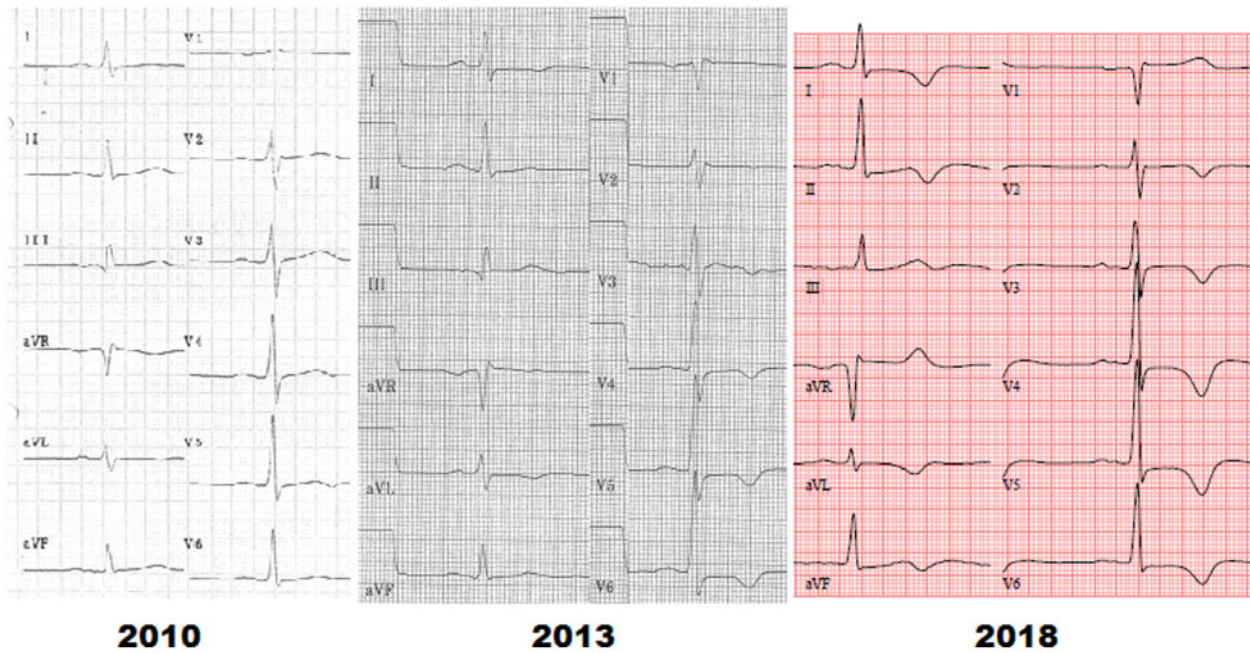
## Case presentation

In 2010, a 57-year-old Caucasian male with a history of hypertension and familial hypercholesterinaemia presented to our outpatient clinic with newly developed tearing left-sided chest pain radiating to the back unrelated to exercise. He was cycling regularly without compromise. His medication included Ramipril, Ezetimibe, and Rosuvastatin. Family history: the patient's mother suffered from an unspecified heart condition since age 40, the father died of a stroke at an older age. His daughter and two granddaughters have no known cardiac condition. The physical examination was

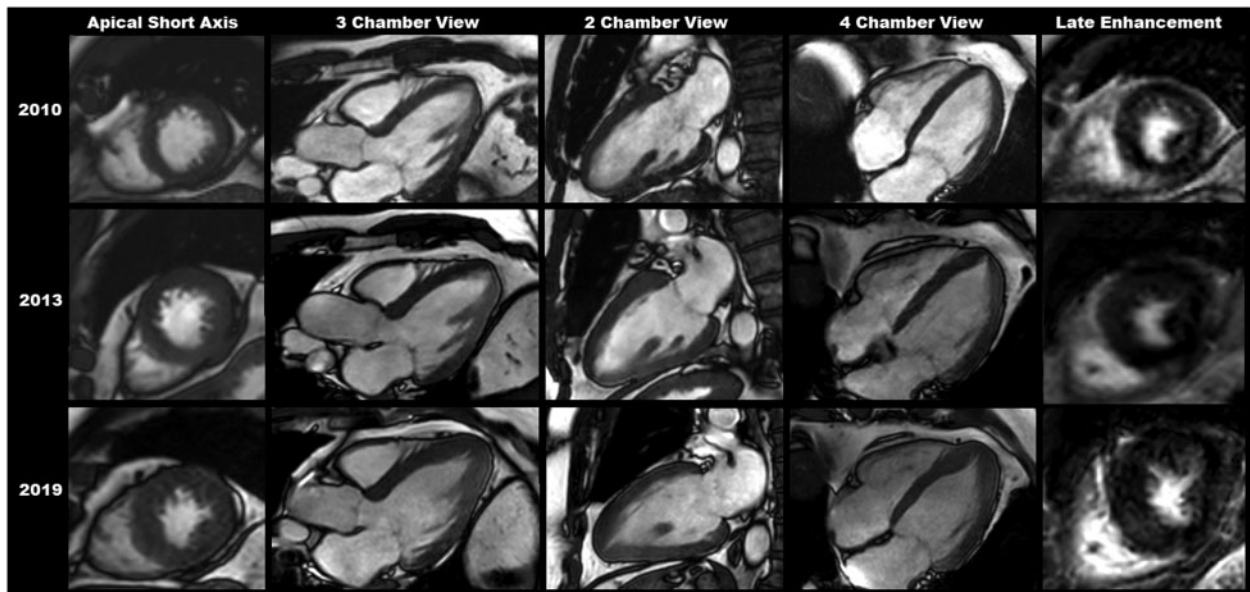
unremarkable, the blood pressure 130/80 mmHg. The resting electrocardiogram (ECG) showed slight T-wave inversions in V5 (Figure 1, left). Troponin I was at 0.1 ng/mL (reference  $<0.032$  ng/mL). A bicycle exercise ECG was terminated early due to ascending ST-segment-depressions and marked hypertension (237/100 mmHg). Transthoracic echocardiography showed a normal left ventricular ejection fraction (LVEF  $>60\%$ ). Cardiac magnetic resonance (CMR) with dobutamine stress showed no signs of ischaemia with an LVEF of 67%. The apical wall thickness was 8 mm with a ratio of 1.1 (Figure 2, top row). In 2013, the patient was referred again for anterolateral T-wave inversions (Figure 1, middle), at this point symptom free. The blood pressure was 140/80 mmHg. Echocardiography suggested slight concentric hypertrophy. A second dobutamine stress-CMR showed no signs of ischaemia. The apical wall thickness had grown to 11 mm, meeting the criteria for relative but not absolute apical hypertrophy (Figure 2, middle row). Subsequent exercise ECGs in 2016 and early 2018 showed the known ST-depressions and exercise-induced hypertension. At the end of 2018, the patient presented again with atypical chest pain and exertional dyspnoea New York Heart Association II (fast cycling, 3–4 flights of stairs). Blood pressure was 166/101 mmHg. The resting ECG showed global T-wave inversions (Figure 1, right). High-sensitive Troponin I was slightly elevated at 4.5 ng/mL (reference  $<1.9$  ng/mL) without a relevant kinetic. Echocardiography showed diastolic dysfunction ( $E/A$  1.5,  $E/E'$  medial 22.0, lateral 15.1, LAVi 35 mL/m<sup>2</sup>) and marked apical hypertrophy (16 mm, ratio 1.8, Figure 3). Coronary artery disease was excluded by coronary angiography. The left ventricular end-diastolic pressure was elevated at 22 mmHg. A third CMR in early 2019 confirmed the apical hypertrophy (Figure 2, bottom row). Late enhancement imaging (Figure 2) and parametric CMR (Figure 4) showed diffuse fibrosis of the apical septum in 2019. Regional and global longitudinal and circumferential endocardial feature-tracking strain values showed progressive impairment of the longitudinal strain in the apical segments (Figure 5) with pathological values at the last exam compared to published reference values.<sup>14,15</sup> A diagnosis of apical HCM was made. Holter monitoring showed no cardiac arrhythmias, 24 h ambulatory blood pressure monitoring showed arterial hypertension (mean 146/90 mmHg, dipper). Verapamil and Chlortalidon were prescribed. Cardiac consultation for the patient's daughter and granddaughters was recommended.

## Discussion

In our case, a previously asymptomatic male presented with symptoms and ECG-changes that led to several diagnostic tests over a time span of 9 years to exclude coronary artery disease until finally the diagnostic criteria for apical HCM were met. As T-wave alterations and symptoms preceded morphologic changes, a single imaging examination was not sufficient to exclude apical HCM in its early stage. While reduced apical tapering can be seen as early as 2010 and relative apical hypertrophy was apparent in 2013, traditional diagnostic criteria for HCM (wall thickness  $\geq 15$  mm) were not met. The relative hypertrophy proceeded to absolute hypertrophy in 2019, supporting the view of relative apical hypertrophy as an early manifestation of apical HCM. This underlines the need for specific



**Figure 1** Serial electrocardiogram tracings (50 mm/s, 10 mm/mV) showed progressive T-wave inversions. Sokolow-Lyon-Index (normal <3.5) 2010: 2.3 mV, 2013: 2.6 mV, 2018: 3.1 mV. QT-time 2010: 360 ms, 2013: 370 ms, 2018: 430 ms.

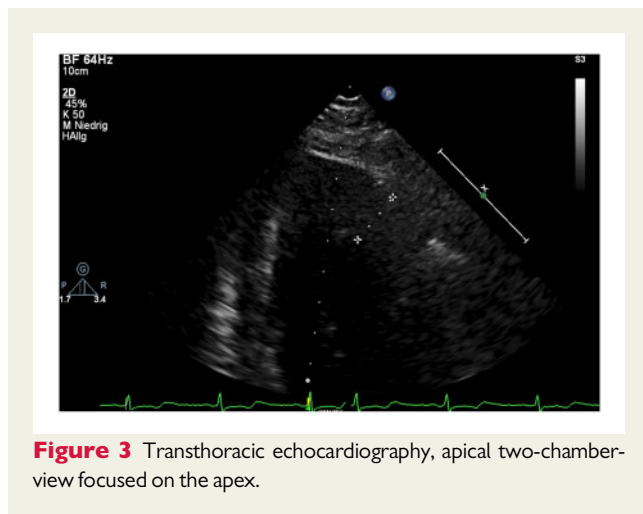


**Figure 2** Serial cardiac magnetic resonances showed progressive apical hypertrophy. Retrospectively, loss of normal apical tapering can be seen as early as 2010.

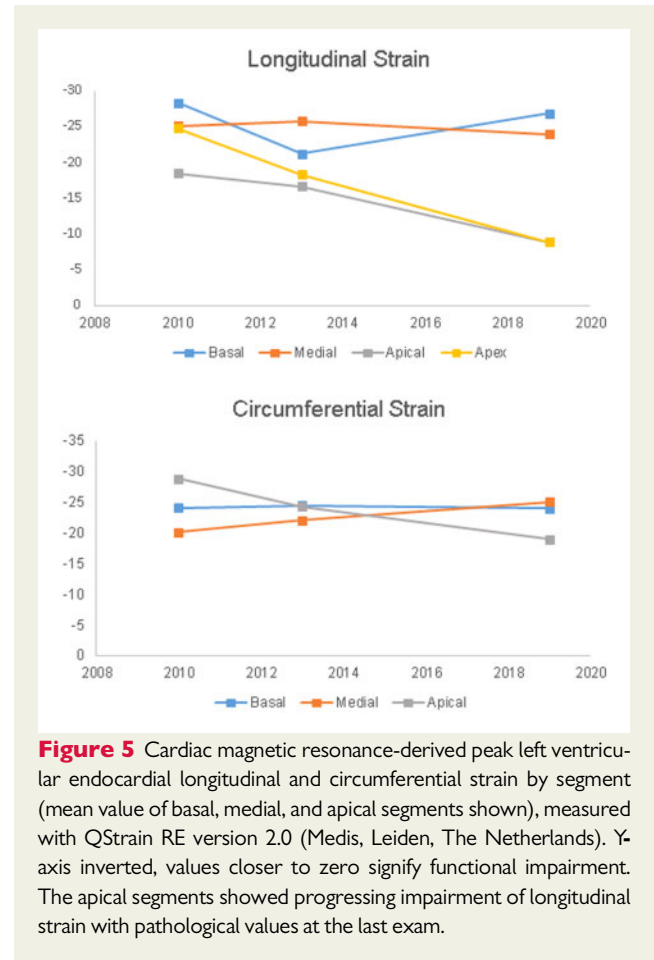
diagnostic criteria for apical HCM, which are not yet addressed in the guidelines of the American and European cardiologic societies. The reason for the late and gradual onset of apical HCM compared to other HCM variants is not established, and available data do not suggest a distinct causative genotype.<sup>13</sup> Compared to non-apical HCM, apical HCM seems to carry a more favourable prognosis.<sup>16</sup> Data on prevention of sudden cardiac death in general HCM are derived from observational studies that did not differentiate by type, and HCM risk calculators might not be reliable in apical HCM.<sup>4</sup> The symptoms of the patient are most likely attributable to microvascular and diastolic dysfunction.<sup>17</sup> While microvascular dysfunction is often detectable on vasodilator stress imaging, this might not be apparent in dobutamine stress imaging.<sup>18</sup>

While no conclusions regarding the sensitivity and specificity of relative apical hypertrophy as a diagnostic criterion for apical HCM can be made from a case report, our findings do encourage further research to determine these. If confirmed in further studies, relative apical hypertrophy in combination with typical ECG changes as a diagnostic criterion for apical HCM would shorten the time from

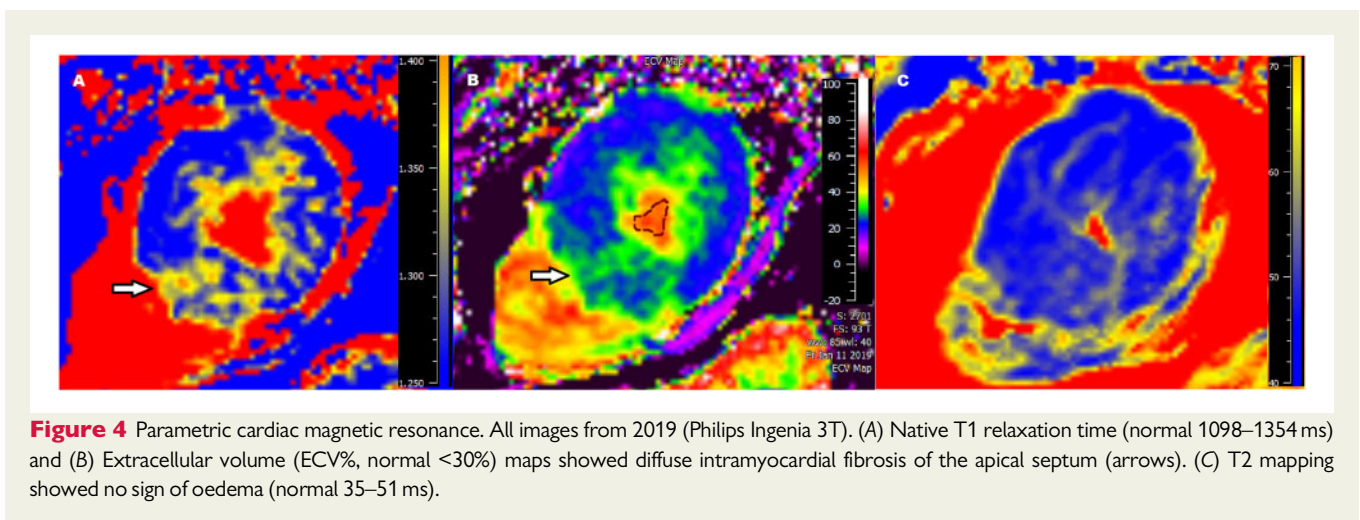
symptom onset to diagnosis and avoid unnecessary ischaemia testing. Relative apical hypertrophy is readily visualized by CMR, which also offers insights into functional and histological changes in the hypertrophied segments.



**Figure 3** Transthoracic echocardiography, apical two-chamber view focused on the apex.



**Figure 5** Cardiac magnetic resonance-derived peak left ventricular endocardial longitudinal and circumferential strain by segment (mean value of basal, medial, and apical segments shown), measured with QStrain RE version 2.0 (Medis, Leiden, The Netherlands). Y-axis inverted, values closer to zero signify functional impairment. The apical segments showed progressing impairment of longitudinal strain with pathological values at the last exam.



**Figure 4** Parametric cardiac magnetic resonance. All images from 2019 (Philips Ingenia 3T). (A) Native T1 relaxation time (normal 1098–1354 ms) and (B) Extracellular volume (ECV%, normal <30%) maps showed diffuse intramyocardial fibrosis of the apical septum (arrows). (C) T2 mapping showed no sign of oedema (normal 35–51 ms).

## Conclusion

Apical HCM is an under-recognized pathology with symptoms and ECG-changes mimicking coronary artery disease that can manifest gradually at a later age in a previously asymptomatic individual. Cardiac magnetic resonance imaging is useful to distinguish apical HCM from other causes of chest pain and ECG changes.

## Lead author biography



Patrick Doebelin, MD, is a cardiologist at the German Heart Centre Berlin in CMR subspecialty training. He graduated from the Charité University Medicine Berlin and completed his general cardiology training at the Charité Campus Benjamin Franklin and the German Heart Centre Berlin. His research interests are CMR tissue characterization and computational approaches to imaging. He is a student of Medical Informatics (distance learning) at the Beuth-Hochschule Berlin.

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## Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidelines.

**Conflict of interest:** B.P. reports having received consultancy and lecture honoraria from Bayer Daiichi Sankyo, MSD, Novartis, Sanofi-Aventis, Stealth Peptides and Vifor Pharma; and editor honoraria from the Journal of the American College of Cardiology. S.K. reports receiving grants from Philips Healthcare and speaker honoraria from Medis. P.D. owns stock of Siemens and Bayer. All other authors declare that they have no financial and non-financial competing interest to disclose.

**Funding:** none declared.

## Acknowledgements

We like to thank Radu Tanacli for the strain measurements.

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