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CASE SERIES
Heart failure

Transient decrease in the depth of the negative T wave in apical hypertrophic cardiomyopathy is a sign of left anterior descending artery stenosis: a case series

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Background In patients with apical hypertrophic cardiomyopathy (HCM), electrocardiography (ECG) often shows left ventricular hypertrophy (LVH) and a negative T wave. A negative T wave often disappears over time due to degeneration of the apical myocardium. However, there are limited reports on the temporary change of a negative T wave in patients with HCM.

Case summary We report three apical HCM patients with LVH and T wave inversion on their previous ECG who showed a temporary decrease in the depth of the negative T wave. All of them had significant stenosis of coronary arteries including the left anterior descending artery (LAD). After revascularization for the LAD lesion, their ECG returned to the previous depth of the negative T wave.

Discussion The cases presented here suggested that a temporary decrease in the depth of the negative T wave in apical HCM patients may be one of the signs of ischaemia in the anterior-apical region caused by severe stenosis of the LAD.

Keywords Hypertrophic cardiomyopathy • Ischaemic heart disease • ECG • Giant negative T wave • Case series

ESC Curriculum 6.5 Cardiomyopathy • 3.2 Acute coronary syndrome • 3.1 Coronary artery disease

Learning points

- In patients with apical hypertrophic cardiomyopathy (HCM), evaluation of regional wall motion abnormality by echocardiography is often challenging, the electrocardiography may be a more sensitive means of detecting abnormalities of the left ventricular apex.
- A transient decrease in the depth of the negative T wave may be a sign of ischaemia in the anterior-apical region in patients with apical HCM.

Introduction

Hypertrophic cardiomyopathy (HCM) is a primary myocardial disease with heterogeneous morphological, functional, and clinical features. Hypertrophic cardiomyopathy is defined by echocardiography or cardiac magnetic resonance imaging as a maximum left ventricular (LV) wall thickness ≥15 mm (≥13 mm if there is a family history of HCM). Apical HCM is a phenotypic variant of HCM in which, left ventricular hypertrophy (LVH) is limited to the level of the apex below the papillary muscle.[1,2]

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In electrocardiography (ECG) for patients with HCM, voltage criteria for LVH and T wave inversion are common findings, and a negative T wave with a depth ≥10 mm, which is called a giant negative T wave (GNT), is a characteristic hallmark of apical HCM.[3,4] In patients with HCM, the GNT often disappears over time due to degeneration of the apical myocardium and that may be a sign of poor prognosis.[2,5] Hence, there are limited reports on the temporary change of a negative T wave in patients with HCM.[6] Here, we present three cases of apical HCM showing a transient decrease in the depth of the negative T wave due to myocardial ischaemia caused by left anterior descending artery (LAD) stenosis.

Timeline

Echocardiography showed LVH and normal LV wall motion without segmental LV hypokinesis, findings that were not significantly different from those in the previous examinations. Laboratory examinations showed a creatinine kinase (CK) level of 107 U/L (normal range of 59–248 U/L) and a high-sensitivity cardiac troponin T (hs-cTnT) level of 0.034 ng/mL (normal range of <0.014 ng/mL).

Therefore, coronary angiography (CAG) was performed that revealed a severe stenotic lesion (99% stenosis) of the mid-LAD, and percutaneous coronary intervention (PCI) was performed with drug-eluting stent (*Figure 1B*). After the intervention for the LAD, his symptom was relieved and ECG showed mild T wave inversion. After 6 months, the T wave returned to a negative T wave with the previous depth (maximum depth of 7 mm in V_5 lead) (*Figure 1A*, right).

Case	Age, sex	Echocardiography	ECG (previous)	ECG (on admission)	Laboratory data	CAG	Treatment	ECG (after treatment)
1	73-year-old, Male	Diffuse LVH in the apex, papillary muscle hypertrophy	LVH, T wave inversion in I, aVL, and V_4–V_6 leads	Disappearance of negative T wave in V_4–V_6 leads	CK 107 U/L, hs-cTnT 0.034 ng/mL	99% stenosis of the LAD	PCI	T wave inversion in I, aVL, and V_3–V_6 leads
2	80-year-old, Male	LVH predominantly involved in the apex, asymmetric septal hypertrophy	LVH, T wave inversion in I, aVL, and V_3–V_6 leads, GNTs in V_4–V_5 leads	Decrease in the depth of the negative T wave in V_3–V_6 leads	CK 112 U/L, hs-cTnT 0.099 ng/mL	90% stenosis of the LAD and chronic total occlusion of the RCA	CABG	T wave inversion in I, aVL, and V_3–V_6 leads
3	77-year-old, Male	LVH in the basal—mid anterior wall and predominantly involved in the apex, papillary muscle hypertrophy	T wave inversion in I, aVL, and V_3–V_6 leads	Decrease in the depth of the negative T wave in I, aVL, and V_3–V_6 leads	CK 122 U/L, hs-cTnT 0.288 ng/mL	99% stenosis of the LAD	PCI	T wave inversion in I, aVL, and V_3–V_6 leads

CAG, coronary angiography; ECG, electrocardiography; LVH, left ventricular hypertrophy; GNT, giant negative T wave, CK, creatinine kinase; hs-cTnT, high-sensitivity cardiac troponin T; LAD, left anterior descending artery; RCA, right coronary artery; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

Case presentation

Case 1

A 73-year-old Japanese male had been followed at our outpatient clinic for apical HCM for 3 years. His previous medical history included dyslipidaemia and polymyositis. There was no family history of cardiovascular disease or sudden cardiac death. In a steady state, he complained of mild exertional dyspnoea with New York Heart Association functional Class II. Electrocardiography shows sinus rhythm, LVH with ST depression, and T wave inversion (maximum depth of 6 mm in V_5 lead) in lateral leads (I, aVL, and V_4–V_6 leads) (*Figure 1A*, left). Echocardiography shows a LV ejection fraction of 72%, diffuse LVH in the apex (maximum LV wall thickness of 15 mm), and papillary muscle hypertrophy (*Figure 2*). These findings were consistent with apical HCM.[1,2]

During follow-up, he was admitted to our outpatient clinic for chest discomfort. On physical examination, the fourth heart sound was auscultated. Electrocardiography shows sinus rhythm and disappearance of the negative T wave in V_4–V_6 leads (*Figure 1A*, middle).

Case 2

An 80-year-old Japanese male was diagnosed as having apical HCM, hypertension, dyslipidaemia, and diabetes mellitus. Electrocardiography shows sinus rhythm and LVH with GNTs in V_4–V_5 leads (10 mm in V_4–V_5 lead) (*Figure 1C*, left). Echocardiography showed a LV ejection fraction of 70%, LVH predominantly involving the apex (maximum LV wall thickness of 18 mm), and asymmetric septal hypertrophy without a gradient. Hs-cTnT level was mildly elevated (0.029 ng/mL) in a steady state. Although he had a history of hypertension, his blood pressure had been controlled well for a long duration, and echocardiographic findings were consistent with HCM rather than hypertensive heart disease.

On a regular outpatient day, he had no symptoms. However, ECG shows sinus rhythm and a decrease in the depth of the negative T wave (7 mm in V_4 lead and 6 mm in V_5 lead) (*Figure 1C*, middle). Echocardiography showed normal LV wall motion without segmental LV hypokinesis, findings that were not significantly different from those in the previous examinations. Laboratory data showed a normal CK level (112 U/L) and an elevated hs-cTnT level (0.099 ng/mL). Coronary

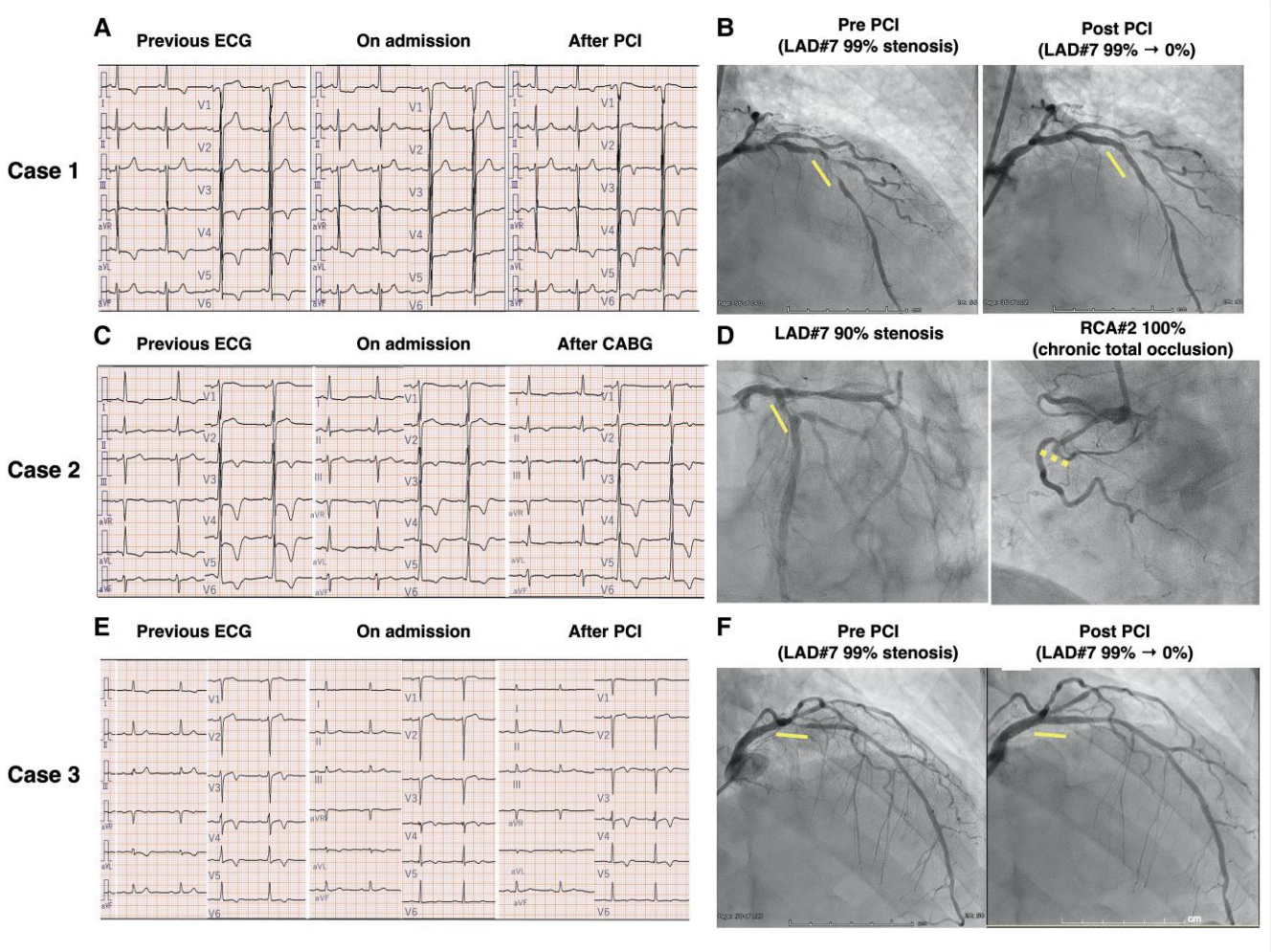

Figure 1 Case 1. (*A*) The previous electrocardiography showed sinus rhythm and left ventricular hypertrophy with T wave inversion in lateral leads (I, aVL, and V_4–V_6 leads) (left panel). When the patient visited our outpatient clinic for exertional dyspnoea, electrocardiography showed the disappearance of the negative T wave in V_4–V_6 leads (middle panel). After performing percutaneous coronary intervention for the left anterior descending artery, electrocardiography returned to left ventricular hypertrophy with a negative T wave (right panel). (*B*) Coronary angiography shows a severe stenotic lesion (99% stenosis) in the left anterior descending artery, and percutaneous coronary intervention was performed for the left anterior descending artery. Case 2. (*C*) Electrocardiography shows sinus rhythm and left ventricular hypertrophy with negative T wave, especially giant negative T waves in V_4–V_5 leads (left panel). On a regular outpatient day, electrocardiography showed a decrease in the depth of the negative T wave (middle panel). After coronary artery bypass grafting, the electrocardiography returned to a baseline negative T wave (right panel). (*D*) Coronary angiography shows three-vessel disease including severe stenosis (90%) of the left anterior descending artery and chronic total occlusion in the right coronary artery. Case 3. (*E*) Electrocardiography shows sinus rhythm with inverted T waves in I, aVL, and V_3–V_6 leads (left panel). At the time of admission because of chest discomfort on exertion, electrocardiography showed decreases in the depth of the inverted T waves (middle panel). After percutaneous coronary intervention, electrocardiography shows that the depth of inverted T waves has returned to the previous level (right panel). (*F*) Coronary angiography shows a severe stenotic lesion in the left anterior descending artery, and percutaneous coronary intervention was performed for the left anterior descending artery. The yellow solid bar shows a stenotic lesion of the coronary artery. The yellow dot bar shows the chronic total occlusion site of the right coronary artery.

angiography shows three-vessel disease including severe stenosis (90%) of the LAD and total occlusion of the right coronary artery (RCA) (*Figure 1D*). Additionally, fractional flow reserve for the LAD lesion under the condition of reactive hyperaemia by the intracoronary administration of nicorandil indicated 0.73 (cutoff value of 0.80) as physiologically significant stenosis.

After a discussion with the heart team about the therapeutic strategy, we decided to perform coronary artery bypass surgery with a left internal thoracic artery graft to the LAD and a saphenous vein graft to the RCA. After the bypass surgery, ECG returned to baseline negative T waves (8 mm in V_4–V_5 leads) (*Figure 1C*, right). He was asymptomatic consistently pre- and post-revascularization. It might be related to his low physical activity level and diabetes mellitus.

Case 3

A 77-year-old Japanese male was previously diagnosed as having apical HCM, hypertension, dyslipidaemia, and diabetes mellitus. He had no family history of cardiovascular disease. Electrocardiography shows sinus rhythm with inverted T waves in I, aVL, and V_3–V_6 leads (maximum

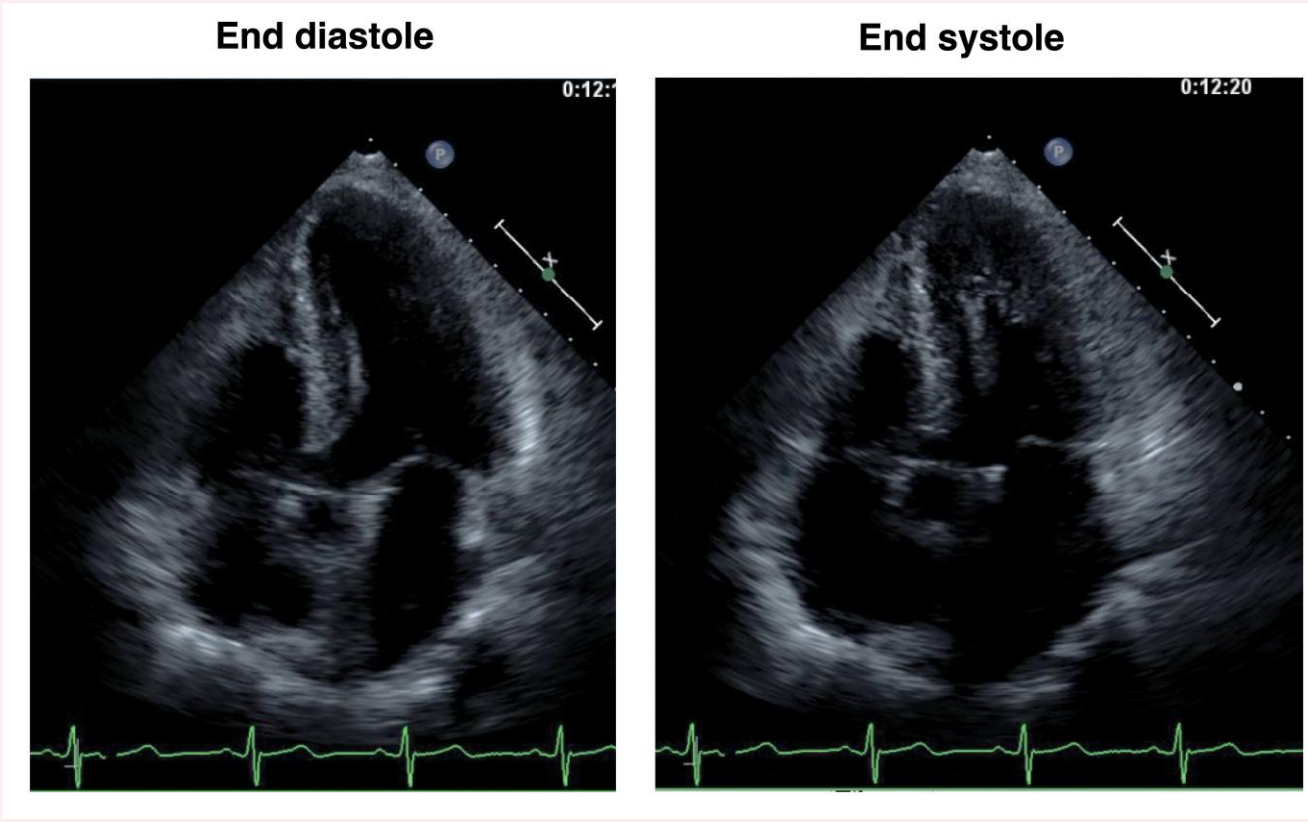

Figure 2 Echocardiography shows a left ventricular ejection fraction of 72% and diffuses left ventricular hypertrophy in the apex and papillary muscle hypertrophy.

depth of 4 mm in V_4 lead) (*Figure 1E*, left). Echocardiography showed a LV ejection fraction of 64% and LVH in the basalmid- anterior wall and predominantly in the apex with papillary muscle hypertrophy (maximum LV wall thickness of 15 mm). The Hs-cTnT level was 0.013 ng/mL in a steady state. He had a history of hypertension, but his blood pressure had been controlled well for a long duration, and echocardiographic findings were suggestive of HCM rather than hypertensive heart disease.

He was admitted to our outpatient clinic for chest discomfort on exertion. Physical examination revealed no remarkable findings. Electrocardiography shows decreases in the depth of inverted T wave in I, aVL, and V_3–V_6 leads (maximum depth of 2 mm in V_4 lead) (*Figure 1E*, middle). Laboratory data showed an elevated hs-cTnT level (0.288 ng/mL) and a normal CK level (122 U/L). Echocardiography revealed LVH and normal LV wall motion without segmental LV hypokinesis. Coronary angiography was performed and revealed a severe stenotic lesion of the proximal LAD (99% stenosis). We immediately performed PCI (*Figure 1F*). After the intervention, his symptom was relieved. Electrocardiography shows that the depth of inverted T waves has returned to the previous level (maximum depth of 4 mm in V_4 lead) (*Figure 1E*, right).

Discussion

To the best of our knowledge, there are limited reports about the temporary change of the negative T wave caused by coronary artery disease in patients with apical HCM.[6] We present three cases of apical HCM that showed temporary disappearance or decrease of the negative T wave associated with ischaemic heart disease including a LAD lesion. After revascularization for the LAD, the T wave returned to a negative T wave with the previous depth, in all cases, several months later.

Apical HCM is a phenotypic variant of HCM in which LVH is limited to the distal apex. Apical HCM was first described by Sakamoto *et al.*[7] and, subsequently, by Yamaguchi *et al.*[8] It is exemplified by unique electrographic findings of giant T wave inversions and echocardiographic features of apical hypertrophy. The prevalence of apical HCM is high in Japan, accounting for ~15% of all HCM cases, compared with the prevalence of 3% in the USA.[9]

Electrocardiography is a sensitive and useful diagnostic tool for HCM. More than three-quarters of HCM patients have abnormal ECG findings such as an abnormal Q wave, ST-T change, negative T wave, and high voltage in precordial leads.[10,11] A negative T wave with a depth ≥10 mm in any lead is defined as a GNT, which is regarded as a relatively typical apical HCM marker.[12] It was reported that LV wall thickness at the papillary muscle and apex levels was greater in apical HCM patients with a GNT than in those without a GNT.[13] The depth of the T wave may vary during the course of the disease. High voltage and GNT often decrease or disappear over time and that may be a sign of poor prognosis.[2,5] It has been speculated that the progression of myocardial disease in the LV apex is a mechanism for the disappearance of GNT in apical HCM patients.[5]

Chest pain and tightness are common symptoms in HCM patients, and they are caused by relative myocardial ischaemia, coronary vasospasms, or coronary artery stenosis.[14] It was reported that the prevalence of coronary artery stenosis in HCM patients ranged from 11 to 26%. Moreover, it was reported that the risk of death was greater in HCM patients with severe coronary artery disease than in HCM patients without the disease.[15,16]

In the setting of non-ST-segment elevation acute coronary syndrome, the characteristic abnormalities of ECG include ST-segment depression

and T wave inversion.[17] T wave inversion in precordial leads is well known as Wellens' syndrome, representing severe stenotic lesions of the LAD.[18] Due to the similar large negative T waves in precordial leads on ECG and similar presenting symptoms of chest pain or chest discomfort, differentiation of these two diseases can be challenging. Several previous reports have indicated that apical HCM might mimic coronary artery disease.[19] In this case series, we showed that apical HCM patients complicated with LAD stenosis could present a decreasing depth of the negative T wave or GNT, unlike patients with Wellens' syndrome.

We could not detect LV wall motion abnormalities by echocardiography in any of the cases. Evaluation of the apex is sometimes difficult due to massive hypertrophy on echocardiography in apical HCM patients.[20] It is possible that ECG is a more sensitive means of detecting abnormality of the LV apex. So, when we encounter the disappearance or decrease of the negative T wave in patients with apical HCM, we should explore the possibility that the ECG change is caused by not only the natural clinical disease course but also severe stenosis of the LAD.

There are some limitations. First, we did not prove functional ischaemia by myocardial perfusion scintigraphy in any of the cases. We considered that revascularization for the LAD should be given priority over an assessment of functional ischaemia because of symptomatic angina with severe stenosis of coronary arteries. Second, we could not evaluate structural abnormalities in the LV apex by cardiac computed tomography or cardiac magnetic resonance imaging.

In this case series, three apical HCM patients showed decreasing depth of the negative T wave or GNT. They showed coronary artery stenosis including severe stenosis of the LAD. After revascularization for the LAD lesion, the T wave negativity returned to its previous depth. In patients with apical HCM, decreasing T wave negativities may be one of the signs of ischaemia of the anterior-apical region due to LAD stenosis.

Conclusion

We reported three apical HCM patients with LVH with T wave inversion on their previous ECG who showed a temporary decrease in the depth of the inverted T wave. There are limited reports on serial ECG changes over time in patients who have apical HCM complicated with ischaemic heart disease. The cases presented here suggested that a temporary decrease in the depth of the inverted T wave may be one of the signs of ischaemia at the anterior-apical region caused by severe stenosis of the LAD.

Lead author biography

Naoki Arima, MD, is a cardiologist at Kochi Medical School. He completed his medical education at Kochi Medical School, Kochi University. He is interested in the field of advanced heart failure and heart transplantation. Now, he is a graduate student conducting research on the immunological mechanisms of myocarditis and cardiomyopathy.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for the submission and publication of this case report, including images and associated text, has been obtained from the patients in accordance with COPE guidelines.

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References

1. Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, *et al.* 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: the task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). *Eur Heart J* 2014;**35**:2733–2779.
2. Kitaoka H, Tsutsui H, Kubo T, Ide T, Chikamori T, Fukuda K, *et al.* JCS/JHFS 2018 guideline on the diagnosis and treatment of cardiomyopathies. *Circ J* 2021;**85**:1590–1689.
3. Eriksson MJ, Sonnenerg B, Woo A, Rakowski P, Parker TG, Wigle ED, *et al.* Long-term outcome in patients with apical hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002;**39**:638–645.
4. Alfonso F, Nihoyannopoulos P, Stewart J, Dickie S, Lemery R, McKenna WJ. Clinical significance of giant negative T waves in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1990;**15**:965–971.
5. Koga Y, Katoh A, Matsuyama K, Ikeda H, Hiyamuta K, Toshima H, *et al.* Disappearance of giant negative T waves in patients with the Japanese form of apical hypertrophy. *J Am Coll Cardiol* 1995;**26**:1672–1678.
6. Iida K, Sugishita Y, Yukisada K, Ito I. Diurnal change of giant negative T wave in patients with hypertrophic cardiomyopathy. *Clin Cardiol* 1990;**13**:272–278.
7. Sakamoto T, Tei C, Murayama M, Ichiyasu H, Hada Y. Giant T wave inversion as a manifestation of asymmetrical apical hypertrophy (AAH) of the left ventricle. Echocardiographic and ultrasono-cardiotomographic study. *Jpn Heart J* 1976;**17**:611–629.
8. Yamaguchi H, Ishimura T, Nishiyama S, Nagasaki F, Nakanishi S, Takatsu F, *et al.* Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): ventriculographic and echocardiographic features in 30 patients. *Am J Cardiol* 1979;**44**:401–412.
9. Kitaoka H, Doi Y, Cassey SA, Hitomi N, Furuno T, Maron BJ. Comparison of prevalence of apical hypertrophic cardiomyopathy in Japan and the United States. *Am J Cardiol* 2003;**92**:1183–1186.
10. Ryan MP, Cleland JG, French JA, Joshi J, Choudhury L, Chojnowska L, *et al.* The standard electrocardiogram as a screening test for hypertrophic cardiomyopathy. *Am J Cardiol* 1995;**76**:689–694.
11. Kubo T, Kitaoka H, Okawa M, Hirota T, Hoshikawa E, Hayato K, *et al.* Clinical profiles of hypertrophic cardiomyopathy with apical phenotype -comparison of pure-apical form and distal-dominant form-. *Circ J* 2009;**73**:2330–2336.
12. Maron BJ, Wolfson JK, Ciró E, Spirito P. Relation of electrocardiographic abnormalities and patterns of left ventricular hypertrophy identified by 2-dimensional echocardiography in patients with hypertrophic cardiomyopathy. *Am J Cardiol* 1983;**51**:189–194.
13. Park SY, Park TH, Kim JH, Baek HK, Seo JM, Kim WJ, *et al.* Relationship between giant negative T-wave and severity of apical hypertrophy in patients with apical hypertrophic cardiomyopathy. *Echocardiography* 2010;**27**:770–776.
14. Kodama K, Hamada M, Kazatani Y, Matsuzaki K, Murakami E, Shigemitsu Y, *et al.* Clinical characteristics in Japanese patients with coexistent hypertrophic cardiomyopathy and coronary vasospasm. *Angiology* 1998;**49**:849–855.
15. Sorajja P, Ommen SR, Nishimura RA, Gersh BJ, Berger PB, Tajik AJ. Adverse prognosis of patients with hypertrophic cardiomyopathy who have epicardial coronary artery disease. *Circulation* 2003;**108**:2342–2348.
16. Shin YJ, Lee JH, Yoo JY, Kim JA, Jeon Y, Yoon YE, *et al.* Clinical significance of evaluating coronary atherosclerosis in adult patients with hypertrophic cardiomyopathy who have chest pain. *Eur Radiol* 2019;**29**:4593–4602.
17. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, *et al.* 2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2021;**42**:1289–1367.
18. de Zwaan C, Bär FW, Wellens HJ. Characteristic electrocardiographic pattern indicating a critical stenosis high in left anterior descending coronary artery in patients admitted because of impending myocardial infarction. *Am Heart J* 1982;**103**:730–736.
19. Abdin A, Eitel I, de Waha S, Thiele H. Apical hypertrophic cardiomyopathy presenting as acute coronary syndrome. *Eur Heart J Acute Cardiovasc Care* 2016;**3**:289–291.
20. Maron BJ, Spirito P, Green KJ, Wesley YE, Bonow RO, Arce J. Noninvasive assessment of left ventricular diastolic function by pulsed Doppler echocardiography in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1987;**10**:733–742.