Apically displaced papillary muscles mimicking apical hypertrophic cardiomyopathy

Seung-Pyo Lee, Kyungil Park, Hyung-Kwan Kim, Yong-Jin Kim, and Dae-Won Sohn

1Cardiovascular Center, Seoul National University Hospital, Seoul, Korea; 2Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea; and 3SNU-Duke Cardiovascular MR Center, 101 Daehak-ro, Jongno-gu, 110-744 Seoul, Korea

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Aims
Apical hypertrophic cardiomyopathy (ApHCM) is a subtype of hypertrophic cardiomyopathy, which is clinically suspected by a characteristic giant negative T (GNT) wave on electrocardiogram (ECG) and diagnosed by demonstrating apical hypertrophy on ECG. However, GNT may not always be specific for ApHCM as in this report of apically displaced papillary muscle (ADPM).

Methods and results
By retrospectively collecting 12-lead ECGs with a GNT wave and apical hypertrophy on 2D-ECG from 2008 to 2010, we identified 55 patients with both of these findings. ADPM was defined to be present when the base of the papillary muscle originated from the apical one-third of the left ventricle. A diagnosis of ApHCM in patients with apical hypertrophy but without evidence of ADPM was given otherwise. Careful evaluations of 2D-ECGs suggested that 20% (11/55) of all patients had an ADPM mimicking ApHCM. Baseline clinical and echocardiography data were not different between the two except for the maximal T wave on 12-lead ECG and apicoseptal hypertrophy, suggesting that the differentiation of these two groups may be subtle and difficult. In addition, patients with ADPM frequently showed abnormal insertion of papillary muscle into the left ventricular outflow tract or into the base of mitral valve leaflet.

Conclusion
These findings suggest that ADPM may also be present with GNT on 12-lead ECG and emphasizes the careful evaluation of the left ventricular apex for proper diagnosis and discrimination of ApHCM.

Keywords
Hypertrophic cardiomyopathy • Papillary muscle displacement • 2D echocardiography

Introduction
Apical hypertrophic cardiomyopathy (ApHCM) is a subtype of hypertrophic cardiomyopathy (HCM), which is more frequently found in Asians than in Caucasians. Although it has been demonstrated that ApHCM is generally benign, cardiovascular complications are not uncommon and therefore, correct diagnosis of this entity is important.

Twelve-lead electrocardiograms (ECGs) of ApHCM are characterized by a giant negative T (GNT) wave in precordial leads. Moreover, the depth of the GNT wave has been reported to be associated with the severity of apical thickening or with the ratio of apical-to-basal myocardial thickness. Therefore, in the presence of a GNT wave, a diagnosis of ApHCM has often been made in patients with apical hypertrophy, especially when the GNT wave cannot be explained otherwise.

However, a notable proportion of patients with a GNT wave and apical hypertrophy referred to our clinic under a diagnosis of ApHCM were later found to have apically displaced papillary muscle (ADPM). In this study, patients with both a GNT wave on 12-lead ECG and apical hypertrophy on 2D-echocardiography were retrospectively collected to determine the incidence and echocardiographic features of ADPM and to clarify the problem associated with the diagnosis of ApHCM.

Methods
Study subjects
From January 2008 to October 2010, patients with a GNT wave on resting 12-lead ECG and echocardiographic evidence of apical hypertrophy were recruited.
The presence of a GNT wave was retrospectively identified using an automated electronic medical record programme. A GNT wave was defined as T wave of $\geq 10$ mm in any precordial lead (Figure 1A). Patients with a bundle branch block, pacing rhythm or a coexisting medical condition other than apical hypertrophy reported to be associated with a GNT wave were excluded.

**Echocardiographic evaluation**

All study subjects had undergone a comprehensive 2D-echocardiographic examination using a 3.5-MHz transducer in a commercially available equipment (Vivid 7, GE Medical Systems, Horten, Norway) and the border of the Left ventricular (LV) endocardium were all clearly delineated at the standard parasternal and apical views. None of the patients underwent contrast echocardiography except for two patients (see Supplementary data online, Video S1 and S2). LV end-diastolic/systolic diameters and wall thicknesses were measured using the standard M-mode tracings in a parasternal short-axis view at the mid-ventricular level and septal/lateral wall thickness at the apical level were measured using parasternal

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**Figure 1** Electrocardiogram and its images of apical hypertrophy. (A) T wave negativity more prominent in the mid-precordial than in the lateral precordial leads represent classic electrocardiographic finding in apical hypertrophy. (B) Representative echocardiography images of the classic pattern of apical hypertrophic cardiomyopathy showing an ‘ace of spade’ shape during diastole. (C) However, it is not unusual to encounter an atypical pattern of hypertrophy showing more prominent hypertrophy at the apical lateral than at the apical septal segments (see Supplementary data online, Video S3).

**Figure 2** Definition of apically displaced papillary muscle. The apically displaced anterolateral papillary muscle was defined when the base of the papillary muscle was located at the apical one-third of the left ventricle.
short-axis 2D images at end diastole. The thickness of the apical segments was measured including the papillary muscle because it was difficult to discriminate between the papillary muscle and the LV myocardium accurately at the apical level of parasternal short-axis images. The peak early (E) and late (A) diastolic velocities of mitral inflow were measured using pulsed-wave Doppler at the tip of the mitral leaflets. The peak early (E') and late (A') diastolic mitral annulus velocities at the septal side were measured in an apical four-chamber view using tissue Doppler imaging. An abnormal LV filling pressure was defined as $E/E' > 15$ as in previous publications and the degree of diastolic dysfunction classified according to the current literature. All echocardiographic measurements were averaged for three beats in sinus rhythm and five beats in atrial fibrillation.

Apical hypertrophy was defined as asymmetric left ventricular hypertrophy predominantly at the apex with a maximal apical wall thickness of ≥15 mm and a maximal apical to posterior wall thickness ratio of ≥1.5 by 2D-echocardiography as previously reported.

Figure 3 Comparison of apically displaced papillary muscle and apical hypertrophy cardiomyopathy. (A) Representative parasternal short-axis and apical images of apically displaced papillary muscle. (B) Representative parasternal short-axis and apical images of apical hypertrophic cardiomyopathy. Note the similar parasternal short-axis images between the two (top two panels), whereas the apical images reveal that papillary muscles appear distinctly different between the two (bottom two panels). PSAX, parasternal short-axis.
Table 1  Baseline clinical characteristics of the study participants

<table>
<thead>
<tr>
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<th>ADPM (n = 11)</th>
<th>ApHCM (n = 44)</th>
<th>P-value</th>
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<tr>
<td>Age</td>
<td>71.5 ± 10.3</td>
<td>61.7 ± 9.6</td>
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<td>Male sex</td>
<td>81.8 (9)</td>
<td>86.4 (38)</td>
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<td>Hypertension</td>
<td>63.6 (7)</td>
<td>72.7 (32)</td>
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<td>Diabetes mellitus</td>
<td>18.2 (2)</td>
<td>20.5 (9)</td>
<td>0.618</td>
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<tr>
<td>Dyslipidemia</td>
<td>36.4 (4)</td>
<td>18.2 (8)</td>
<td>0.182</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>I 63.6 (7)</td>
<td>77.3 (34)</td>
<td>0.245</td>
</tr>
<tr>
<td></td>
<td>II 36.4 (4)</td>
<td>15.9 (7)</td>
<td></td>
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<tr>
<td>SBP (mmHg)</td>
<td>132.9 ± 11.9</td>
<td>126.6 ± 15.6</td>
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<tr>
<td>DBP (mmHg)</td>
<td>76.6 ± 7.9</td>
<td>78.4 ± 10.8</td>
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<tr>
<td>Cr (mg/dl)</td>
<td>1.1 ± 0.3</td>
<td>1.1 ± 0.2</td>
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<td>Atrial fibrillation</td>
<td>18.2 (2)</td>
<td>11.4 (5)</td>
<td>0.429</td>
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<td>Maximal height of R wave on ECG (mm)</td>
<td>43.4 ± 12.0</td>
<td>39.1 ± 11.6</td>
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<tr>
<td>Maximal depth of T wave on ECG (mm)</td>
<td>12.5 ± 2.3</td>
<td>14.6 ± 5.3</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Data are presented as mean values ± SD or %. The exact number of patients in each group is presented in the parenthesis. NYHA, New York Heart Association; SBP/DBP, systolic/diastolic blood pressure; Cr, creatinine.
P-values calculated with the t-test or χ²-test as appropriate.

(Figure 1B and C, see Supplementary data online, Video S3 for Figure 1E).23–6

Definition of ADPM

The anterolateral papillary muscle can be easily identified in the apical four-chamber view with minor modification, and its insertion to the anterior mitral valve leaflet can be traced. We identified the papillary muscle as the anterolateral one because the origin of these muscles was all at the lateral segments. ADPM was defined to be present when the base of the papillary muscle originated from the apical one-third of the left ventricle in the apical four-chamber view, irrespective of concomitant hypertrophy in any of the apical segments (Figure 2). A diagnosis of ApHCM in patients with apical hypertrophy but without the evidence of ADPM was given otherwise. In patients with concomitant hypertension, all patients had hypertrophy of the myocardium that was not justified by the degree of hypertension. In addition, no patient was on more than two anti-hypertensive medications. As seen in Figure 3, although there seems to be apical hypertrophy in both identities (parasternal short-axis view in Figure 3A and B), careful examination of the apical views demonstrates that the ADPM is responsible for the apical hypertrophy in Figure 3A, whereas the hypertrophy of the apical myocardium itself is for Figure 3B. The differentiation of ADPM and ApHCM was performed by two investigators (S.-P.L and D.-W.S), the discrimination of which was done independently.

Statistical analysis

Continuous and dichotomous variables are presented as means ± SDs or as percentages, and were compared using Student’s t-test or the χ²-test, respectively. All analysis was performed using SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA), and two-tailed P-values of < 0.05 were considered statistically significant.

Results

From January 2008 to October 2010, 55 patients were found to have a GNT wave on resting 12-lead ECG and apical hypertrophy by echocardiography. A careful analysis of 2D-ECGs demonstrated that 20% (11/55) of the patients could be categorized as ADPM. Comparisons of underlying baseline characteristics revealed no significant difference between the two groups, except for a marginal difference in the negative T wave amplitude on 12-lead ECG (Table 1). Furthermore, no significant difference was observed between these two groups in terms of baseline echocardiographic parameters, except for the thickness of apico-septal segment (Table 2).

A close examination of the 2D-ECG revealed that there exist several variations in the numbers and shapes of papillary muscles...
and of their insertion site (Figure 4 and see Supplementary data online, Video S3 cited in Figure 1 for the normal location of papillary muscle seen in the apical four-chamber view). Although patterns E and F could evoke controversy with respect to the structure designating as papillary muscle, we considered it prudent to refer to it as the papillary muscle rather than an ‘aberrant muscle band’ because the base of this structure is close to or merged with the base of the normal anterolateral papillary muscle, that is, it could be argued that such papillary muscles have two heads. When the insertion site of the papillary muscle was traced in these patients, five showed papillary muscle without apparent chordae inserting into the base of the anterior mitral valve leaflet and two showed papillary muscle directly inserting to the LV outflow tract (LVOT) (Figure 5).

**Discussion**

ApHCM, which is more frequently encountered in Asian than in Caucasians, is characterized by a distinct GNT wave in precordial leads. GNT is believed to be a consequence of repolarization abnormality caused by a thickened myocardium at the apex, i.e. apical hypertrophy on 2D ECGs. However, the most important finding of this study indicates that the conventional criteria used to diagnose ApHCM might include inhomogeneous groups of patients. This may be important because inhomogeneity in the ‘so-called’ ApHCM may profoundly affect treatment guidelines suggested in the previous reports and our understanding of prognosis.

**Subtle electrocardiogram and echocardiography difference between ApHCM and ADPM**

A GNT wave in precordial leads can also be seen in the presence of solitary papillary muscle hypertrophy. Specifically, ~15% of solitary papillary muscle hypertrophy cases were found to be associated with the GNT wave. However, in this previous study, other parts of the LV had normal thickness, whereas patients included in the present study showed an increase in the wall thickness at the apex, which led to a diagnosis of apical hypertrophy. Therefore, an abnormal origin, rather than hypertrophy of the papillary muscle, might have caused the GNT waves observed in the present study.

A low E’ velocity and an elevated E/E’ ratio, representing relaxation abnormality and an elevated LV filling pressure, respectively, were common in both ApHCM and ADPM, despite an insignificant difference in age. An LV apicoseptal wall thickness and a maximal T wave inversion amplitude were numerically higher in the ApHCM group compared with the ADPM group, suggesting that ADPM may be a different entity from ApHCM. However, there were no significant differences in the various echocardiographic parameters between the two entities, suggesting that the discrimination between the two may be subtle. It also emphasizes the role of careful examinations of the 2D images itself and possibly, LV opacification with contrast agent may enable the discrimination between the two.
In the present study, abnormal insertion of the papillary muscle was noted in some patients with ADPM. Some patients had papillary muscle inserted into the base of a mitral leaflet or directly into the LVOT. Furthermore, a subgroup of these patients could possibly have significant LVOT obstruction as has been previously reported.10

Limitations

Our findings are not without limitations, which include a small sample size and a lack of prospective data collection. Indeed, there may have been ADPM patients without GNT, which obscures the true incidence of ADPM. In addition, we could not suggest whether ADPM has any clinical implication, i.e. we could not provide any meaningful clinical follow-up data. Accordingly, the findings of our analysis should be regarded as hypothesis generating and the clinical meaning of this possible new entity should be sought in the future.

In conclusion, we describe a possible unique entity of ADPM that may mimic ApHCM on 12-lead ECGs and ECGs. However, a careful analysis of 2D-echocardiogram may aid in the differentiation of these two entities. Further investigations are warranted to define the clinical meaning of this new entity.

Supplementary data

Supplementary data are available at European Heart Journal – Cardiovascular Imaging online.

Conflict of interest: none declared.

Funding

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References


Significance of focusing on papillary muscle structure in the diagnosis of ADPM

Although patients with ADPM generally showed more prominent hypertrophy at the apicolateral than in the apicoseptal segments, it was also not uncommon to encounter patients showing isolated apicolateral hypertrophy as in Figure 2 (see Supplementary data online, Videos S2 and S4). These echocardiographic features make ADPM difficult to differentiate from ApHCM by the pattern of apical hypertrophy alone, because these two entities look rather similar in the standard parasternal short-axis view (Figure 3). Although one can argue that a certain proportion of ADPM in our study may represent ApHCM with coincidental ADPM, the representative figures shown in our pictures (Figure 3A and see Supplementary data online, Videos S2 and S4) clearly demonstrate that it is not the papillary muscle thickness but the location of the papillary muscle itself that leads to the obliteration of the LV apex at end systole. Also, the echocardiography of ADPM patients nearly never had concomitant apicoseptal hypertrophy, which is in contrast to a majority of ApHCM patients having concomitant apicoseptal hypertrophy.

In Figure 5 Common variations in insertion in ADPM. (A) The papillary muscle inserted into the base of a mitral valve leaflet; arrow: the insertion site of the papillary muscle at the base of the leaflet; arrowhead, mitral valve leaflet. (B) The papillary muscle, which could also be called an aberrant muscle band, inserted directly into the left ventricular outflow tract.

**Figure 5** Common variations in insertion in ADPM. (A) The papillary muscle inserted into the base of a mitral valve leaflet; arrow: the insertion site of the papillary muscle at the base of the leaflet; arrowhead, mitral valve leaflet. (B) The papillary muscle, which could also be called an aberrant muscle band, inserted directly into the left ventricular outflow tract.

Image Focus

An unexpected quadricuspid aortic valve revealed by multislice computed tomography

David Pesenti Rossi*, Raphaëlle Convers, Christian Hubert, and Bernard Livarek

Department of Cardiology and Radiology, Versailles Hospital, Le Chesnay, France

*Corresponding author. Tel: +33 1 3963 8867; fax: +33 9 8170 9491, Email: david.pesentirossi@gmail.com

We report a case where a 58-year-old woman with no significant past medical history presented with chest pain. Clinical examination of heart sounds revealed an aortic incompetence. The electrocardiogram (ECG) and plasma levels of cardiac troponin I were normal. Trans-thoracic echocardiography was performed and revealed a normal left ventricular function and no pericardial effusion, a medium aortic incompetence (arrow) but aortic valve morphology could not be assessed (Panels 1 and 2) even in the short-axis. Cardiac multislice computed tomography (MSCT) was performed with an ECG-gated acquisition in order to rule out a coronary atherosclerosis. MSCT reconstructions (Panels 3 and 4) revealed a quadricuspid aortic valve with three equal cusps including one right coronary cusp (A), one left coronary cusp (B), a non-coronary cusp (C), and one smaller accessory cusp (D) with a central incompetence (arrow). On the other hand, MSCT (Panels 5 and 6) showed a right coronary second segment significant stenosis (star). Therefore, conventional angiography confirmed the right coronary significant stenosis which was treated by stent. The aortic regurgitation did not require surgical treatment but a close follow-up.

Quadricuspid aortic valve is a rare congenital cardiovascular disorder. Only a few cases have been reported in the literature. This pathology often leads to aortic valve regurgitation that requires surgical treatment. This case illustrates multiple MSCT benefits, a characterization of native cardiac valves with inadequate images from other non-invasive methods and a coronary evaluation in this patient with intermediate risk of coronary disease presenting with acute chest pain and both negative enzymes and ECG.

Conflict of interest: none declared.

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