The association between T wave inversion and apical hypertrophic cardiomyopathy

Cheol Byoung Chae¹, Ju Hee Ha¹, Jun Ho Kim¹, Jae Joon Lee¹, Han Il Choi¹, Ki Beom Park¹, Jin Hee Kim¹, Jung Hyun Choi²

¹Division of Cardiology, Department of Internal Medicine, Busan medical center, Busan, Korea
²Division of Cardiology, Department of Internal Medicine, Pusan National University Hospital, Busan, Korea

Objectives: Electrocardiography (ECG) is the first step in hypertrophic cardiomyopathy (HCMP) diagnosis. For various reasons, the T wave inversion (TWI) and ECG change with time and HCMP is not easy to diagnosis. The aim of this retrospective study was to investigate the association between TWI on ECG and apical HCMP. Methods: A total of 4,730 ECGs presenting TWI from January 2011 to March 2013 in Pusan National University Hospital were enrolled. 133 patients who were examined by both echocardiography and coronary angiogram were analyzed. Patients were divided into two groups: Group A (TWI ≥ 10 mm) and Group B (5 mm ≤ TWI < 10 mm). HCMP is defined by a wall thickness ≥ 15mm in one or more LV myocardial segments. Apical HCMP is defined to be hypertrophy that is confined to LV apex. The patients who had ECGs with at least one month interval were divided 3 groups: Normal T wave, Abnormal T wave, and Persistent TWI. The prevalence of Apical HCMP and coronary artery disease (CAD) was reviewed among the three groups. Results: In this study there were a total 133 patients, with patients divided into Group A which had 15 patients and Group B which had 118 patients. Among the 23 patients with apical HCMP, three patients were Group A and twenty patients were Group B (P = 0.769). Regarding constancy of TWI, persistent TWI group was higher in apical HCMP than in other groups (P = 0.038). CAD had no difference between groups (P = 0.889). Conclusions: T wave negativity was not associated with incidence of apical HCMP. However, apical HCMP was diagnosed more frequently in patients with persistent TWI. Further follow up echocardiographic study is needed to evaluate the progression of apical HCMP in patients with TWI.

Key Words: Coronary artery disease, Echocardiography, Electrocardiography, Hypertrophic cardiomyopathy, T wave inversion

Apical hypertrophic cardiomyopathy was first reported by Sakamoto of Japan in 1976.¹ As one of the hypertrophic cardiomyopathies, it is characterized by myocardial hypertrophy limited to the left ventricular apex, a giant T wave inversion (T wave inversion ≥ 10 mm) in precordial leads, and a spade shape at the end of diastolic phase of left ventricle due to severe hypertrophy of the left ventricle.² According to recent guidelines, it is indicated by a myocardial thickness greater than...
The association between T wave inversion and apical hypertrophic cardiomyopathy

15 mm on any imaging tests and is indescribable with other underlying disease.³

Apical hypertrophic cardiomyopathy has been reported to have a relatively positive prognosis. However, according to recent studies, clinical complications such as atrial fibrillation, ventricular arrhythmia, myocardial infarction and stroke may occur.⁴,⁵ Therefore, the importance of early diagnosis and active treatment of apical hypertrophic cardiomyopathy is increasingly evident.

T wave inversion on electrocardiography is a characteristic finding of apical hypertrophic cardiomyopathy but T wave inversion can be caused by cardiac or non-cardiac causes.⁷ In addition, T wave inversion may not occur in all apical hypertrophic cardiomyopathy.⁸ The purpose of this study was to investigate the role of electrocardiography in the diagnosis of patients with apical hypertrophic cardiomyopathy by examining the association between T wave inversion and apical hypertrophic cardiomyopathy.

MATERIALS AND METHODS

Among the electrocardiographs (ECGs) performed at the Pusan National University Hospital from January 2011 to March 2013, 4730 ECGs showing T wave inversion from 292 patients were reviewed retrospectively. T wave inversion was defined as the deepest area of the T wave amplitudes with 5 mm or more inversion in the JT segment, except for inversion of 5 mm or less. As mentioned, there were 292 patients who had T wave measurements meeting the above conditions. Among them, 224 patients (76%) underwent echocardiography and 151 patients (51.5%) underwent angiocardiography. 133 patients had both tests and this group were selected in this study.

Patients in this group were divided into two groups depending on the degree of T wave inversion: Group A (T wave inversion ≥ 10 mm) and Group B (T wave inversion ≥ 5 mm). For all 133 patients, the current ECG was compared with previous ECG patterns. Previous ECGs had an interval of at least one month and were divided into: Normal T wave (Normal), Abnormal T wave (Not a T wave inversion of 5 mm or more but abnormal), Persistent TWI (With the same T wave inversion), and 30 cases where no previous ECG was performed (Fig. 1).

Arrhythmia is defined as ventricular and atrial arrhythmia, and valvular disease is defined as moderate to severe reflux or stricture. Non-cardiac disease is defined as any disease other than cardiac disease for main treatment at the time of ECG. In addition, the association between T wave inversion and coronary artery disease, which is one of the common causes of T wave inversion, was analyzed. Coronary artery disease was defined as the presence of more than 50% of coronary stenosis on the angiocardiography or tomographic images.

Transthoracic Echocardiography

Based on 2014 ESC guidelines, apical hyper-
trophic cardiomyopathy was defined as when myocardial hypertrophy was limited to the cardiac apex and the end-diastolic thickness was 15 mm. For echocardiography an iE33 (Phillips Medical System, Andover, MA, USA) or an ACUSON SC 2000 (Siemens Medical Solutions USA Inc., Mountain View CA) were used.

Statistical Analysis
Continuous variables were expressed as mean ± SD and categorical variables were expressed as percentage (%). For statistics, the chi square test or fisher’s exact test was used. A p-value of ≤ 0.05 was considered as statistically significant. SPSS 18.0 (IBM Corp. Armonk, NY, USA) was used for statistical analysis.

RESULTS

Basic Clinical Characteristics (Table 1). Of the 133 patients, 81 patients were male and the mean age was 67.62 ± 9.91 years. Of them, there were 15 patients with 10 mm or greater T wave inversion, 10 patients with 5 mm or greater, and 118 patients with 10 mm or less. Arrhythmia was observed in 11 patients, including atrial fibrillation (9 patients), complete atrioventricular block (1 patient) and sick sinus syndrome (1 patient). Valvular disease was observed in 13 patients, including aortic valve regurgitation (3 patients), aortic stenosis due to a bicuspid aortic valve (2 patients), tricuspid valve regurgitation (3 patients), mechanical valve (1 patient), or mitral regurgitation (4 patients).

T Wave Inversion and Apical Hypertrophic Cardiomyopathy and Coronary Artery Disease (Table 2).
Patients who showed apical hypertrophic cardiomyopathy on transthoracic echocardiography consisted of 3 patients (20%) in Group A and 20
patients (16.9%) in Group B (P = 0.769). Patients with coronary artery disease on angiography consisted of 9 patients (60%) in Group A and 73 patients (61.9%) in Group B (P = 0.889).

The prevalence of apical hypertrophic cardiomyopathy and coronary artery disease with continuous ECG changes (Table 3).

Of 23 patients with apical hypertrophic cardiomyopathy, three patients (13%) showed Normal T wave and three patients (13%) showed abnormal T wave. Eleven patients (47.8%) showed Persistent TWI, which was statistically significant in the patient group with apical hypertrophic car-

Table 1. Basic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 15)</th>
<th>Group B (n = 118)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67.9 ± 9.7</td>
<td>65.8 ± 11.9</td>
<td>0.451</td>
</tr>
<tr>
<td>Male (%)</td>
<td>10(66.7)</td>
<td>71(60.2)</td>
<td>0.630</td>
</tr>
<tr>
<td>DM (%)</td>
<td>3(20)</td>
<td>25(21.2)</td>
<td>0.916</td>
</tr>
<tr>
<td>HTN (%)</td>
<td>5(33.3)</td>
<td>53(44.9)</td>
<td>0.398</td>
</tr>
<tr>
<td>Arrhythmia (%)</td>
<td>0(0)</td>
<td>11(9.3)</td>
<td>0.220</td>
</tr>
<tr>
<td>VHD (%)</td>
<td>0(0)</td>
<td>13(11.0)</td>
<td>0.179</td>
</tr>
<tr>
<td>Vascular disease (%)</td>
<td>2(13.3)</td>
<td>11(9.3)</td>
<td>0.625</td>
</tr>
<tr>
<td>Non cardiac disease (%)</td>
<td>5(33.3)</td>
<td>31(26.3)</td>
<td>0.565</td>
</tr>
</tbody>
</table>

DM : diabetes mellitus, HTN : hypertension, VHD : valvular heart disease

Table 2. The prevalence of apical HCMP and CAD in patients with TWI

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 15)</th>
<th>Group B (n = 118)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCMP</td>
<td>3(20.0)</td>
<td>26(22.0)</td>
<td>0.579</td>
</tr>
<tr>
<td>Apical HCMP (%)</td>
<td>3(20.0)</td>
<td>20(16.9)</td>
<td>0.769</td>
</tr>
<tr>
<td>Other HCMP</td>
<td>0(0.0)</td>
<td>6(5.1)</td>
<td>0.419</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>9(60.0)</td>
<td>73(61.9)</td>
<td>0.889</td>
</tr>
<tr>
<td>LM (%)</td>
<td>0(0)</td>
<td>5(4.2)</td>
<td>0.416</td>
</tr>
<tr>
<td>LAD (%)</td>
<td>9(60.0)</td>
<td>64(54.2)</td>
<td>0.673</td>
</tr>
<tr>
<td>LCX (%)</td>
<td>1(6.7)</td>
<td>29(24.6)</td>
<td>0.118</td>
</tr>
<tr>
<td>RCA (%)</td>
<td>1(6.7)</td>
<td>28(23.7)</td>
<td>0.132</td>
</tr>
<tr>
<td>Spasm, bridge (%)</td>
<td>1(13.3)</td>
<td>8(6.8)</td>
<td>0.428</td>
</tr>
<tr>
<td>Insignificant CAD (%)</td>
<td>5(33.3)</td>
<td>37(31.4)</td>
<td>0.877</td>
</tr>
</tbody>
</table>

HCMP : hypertrophic cardiomyopathy, CAD : coronary artery disease, LCA : left coronary artery, LM : left main, LAD : left anterior descending artery, LCX : left circumflex artery, RCA : right coronary artery
diomyopathy ($P = 0.038$).

Of the 133 patients, 36 patients were not diagnosed with either apical hypertrophic cardiomyopathy or coronary artery disease and among them, 9 patients (25%) showed persistent TWI.

The median follow-up period of ECG was 29 ± 38.4 months.

**DISCUSSION**

Apical hypertrophic cardiomyopathy is a type of hypertrophic cardiomyopathy, in which myocardial hypertrophy is limited to the cardiac apex. On ECG, giant T wave inversion in precordial leads and high voltage QRS waves were observed, and it was characterized by a spade shape in left ventriculography. In many studies, the giant T wave inversion is defined as $\geq 10$ mm of the inverted T wave in any leads.

Since some of the patient’s symptoms include chest pain, dyspnea and palpitation which are similar to angina pectoris, this sometimes causes confusion in the diagnosis. In these patients, myocardial ischemia may occur, although coronary angiography may be normal. Myocardial ischemia is a small vessel disorder with reduced ability for vasodilation, and it is also explained as an imbalance of demand and supply, delayed relaxation of myocardium, reduction of coronary perfusion pressure, and a reduced ratio of capillary and myocardial fibers.

Of the hypertrophic cardiomyopathies, apical hypertrophic cardiomyopathy exhibits relatively positive prognosis, but the risk of acute cardiac arrest, fatal arrhythmia, heart failure and ischemia is increased. In Japan, there is a concern that fatal arrhythmia such as ventricular tachycardia is also more likely to occur.

Many diagnostic tools have been used to avoid these risks, but there is no optimal standard diagnostic method. Echocardiography is widely used for all kinds of hypertrophic cardiomyopathy including apical hypertrophic cardiomyopathy. Apical hypertrophic cardiomyopathy is diagnosed when the thickness of cardiac apex is $> 15$ mm on any type of imaging tests. Recently, it has been shown that the thickness of the myocardium can...
be accurately measured by cardiac magnetic resonance imaging, and even if there is fibrosis of the myocardium, it accurately represents the anatomical features. It has also been reported that the use of contrast enhanced echocardiography can improve the diagnostic accuracy of patients with apical hypertrophic cardiomyopathy.

Although there are diagnostic methods available using these various imaging techniques, sometimes ECG abnormalities may be the first and only diagnostic method. However, the diseases associated with T wave inversion are many and diverse such as: left ventricular anterior wall ischemia, acute central nervous system diseases, stress myocardial infarction, pulmonary edema, antiarrhythmics, pulmonary embolism, cardiac memory due to temporary tachycardia, after pacing, and use of cocaine. Therefore, it is necessary to analyze the T wave inversion which is the main characteristic of apical hypertrophic cardiomyopathy.

The mechanism by which T wave inversion occurs on electrocardiogram is uncertain in apical hypertrophic cardiomyopathy. However, its cause may be attributed to secondary repolarization due to myocardial hypertrophy, myocardial ischemia and metabolic demands due to the hyperdynamic left ventricle.

There are several studies on the relationship between T wave inversion of ECG and apical hypertrophic cardiomyopathy, but the relation is unclear. There was a study reported that the absolute value of the thickness of cardiac apex determines the degree of T wave inversion. Another study showed that the ratio of left ventricular apex/septal wall thickness and cardiac apex/basal myocardial mass ratio were higher in apical hypertrophic cardiomyopathy with giant T wave inversion. According to a study published by Morimoto et al., 43.9% of patients with giant T wave inversion showed the spade shape on ventriculography, and in patients with no T wave inversion, only 7% had apical hypertrophic cardiomyopathy. However, in another recent study, T wave inversion was not found to be an absolute factor in the diagnosis of apical hypertrophic cardiomyopathy.

Because it is important to diagnose apical hypertrophic cardiomyopathy in a noninvasive and easy way, this study was designed using electrocardiogram and echocardiography. Patients with suspected apical hypertrophic cardiomyopathy were screened by electrocardiogram and this was compared with the echocardiographic findings. Since clinically the most commonly considered cause of T wave inversion is coronary artery disease, its incidence was also analyzed.

The absolute value of T wave inversion was not a significant index for diagnosing apical hypertrophic cardiomyopathy, but the prevalence of apical hypertrophic cardiomyopathy was higher in patients group with T wave inversion.

In addition, ECG changes according to various clinical conditions, but there is a lack of analysis on continuous ECG changes. Most previous studies have analyzed cases in which the T wave in-
version was lost or not seen in apical hypertrophic cardiomyopathy. As shown in Table 3, among 23 patients with hypertrophic cardiomyopathy, there were 6 patients with normal T wave and abnormal T wave in the previous ECG results. In all of these cases, the echocardiogram showed hypertrophic cardiomyopathy from the time of observation, and there was no case of newly developed hypertrophic cardiomyopathy following a previously diagnosed normal condition. Among them, one patient had flat T wave, which showed severe stenosis in three coronary arteries and left ventricular systolic dysfunction. Two patients had right heart failure and right atrial enlargement accompanied by severe tricuspid regurgitation. One patient had a bicuspid aortic valve which looked like severe aortic stenosis. In other studies, the long-term follow-up showed that the absolute value of the giant T wave inversion was decreased with the occurrence of accompanying disease such as loss of giant T wave inversion, ischemic heart disease, dilated cardiomyopathy and decreased cardiac contractility, and follow-up studies using magnetic resonance imaging showed a decrease in the absolute value of the T wave inversion when myocardial hypertrophy was moved from cardiac apex to base.

In patients with T wave inversion, 36 patients had neither apical hypertrophic cardiomyopathy nor coronary artery disease, and 9 of those patients had continuous T wave inversion. These patients may have developed an apical hypertrophic cardiomyopathy, so close follow-up is needed. For T wave inversion, persistence was related to the prevalence of apical hypertrophic cardiomyopathy, not severity. However, change to the T wave inversion is also significant because it has the possibility of developing into apical hypertrophic cardiomyopathy. Therefore, for patients with T wave inversion on ECG, an echocardiography follow-up should be required and performed consecutively.

The limitations of this study include the following: repeat tests were not performed in consideration of the variability of ECG over time; in the comparison of multiple electrocardiograms, echocardiography was not performed repeatedly; data on other characteristics such as symptoms according to retrospective studies was not obtained; ECG readout was carried out by one investigator; and the study did not consider the consistency of interobservers and intraobservers.

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335


