The Electrocardiogram as a Diagnostic Tool for Hypertrophic Cardiomyopathy: Revisited

Barry J. Maron, M.D.

Minneapolis Heart Institute Foundation, Minneapolis, Minnesota

Hypertrophic cardiomyopathy (HCM) is a heterogeneous genetic disease that has fascinated cardiologists for more than 4 decades.¹⁻⁸ At present, about 150 mutations in 10 genes have been identified to cause HCM, each encoding proteins of the cardiac sarcomere. Traditionally, the clinical assessment of HCM has relied largely on noninvasive diagnostic testing, principally with echocardiography as well as 12-lead electrocardiography (ECG).

Since the 1970s, with the advent of M-mode and two-dimensional imaging, echocardiography has been established as the "gold standard" for identifying the clinical phenotype of HCM, conventionally defined as unexplained and asymmetric left ventricular (LV) wall thickening associated with a nondilated chamber in the absence of another disease capable of producing hypertrophy of that magnitude.⁸ The HCM⁷ phenotype incorporates a diverse array of patterns in which virtually any distribution or extent of LV wall thickening has been described as part of the broad disease spectrum.^{7,9} More recently, other noninvasive techniques such as magnetic resonance imaging have emerged to be included within the diagnostic armamentarium.

HISTORICAL CONTEXT

The 12-lead ECG substantially predates echocardiography as a diagnostic test in cardiology and has always been of interest to cardiovascular specialists and students of HCM due to the often dramatic (or even bizarre) ECG patterns that may be observed in this disease, some of which mimic myocardial infarction and thereby create diagnostic confusion.⁹⁻¹⁶ ECG abnormalities in HCM most

commonly include markedly increased precordial and standard lead voltages, alterations in the ST segments and T waves including deep T-wave inversion, pathologic deep and narrow Q waves, and conduction abnormalities such as left anterior hemiblock.⁹⁻¹⁷

The ECG is abnormal in 75% to 95% of HCM patients^{1,12,17-19} and normal ECGs are most commonly encountered in family members identified as part of pedigree screening when associated with mild localized LV hypertrophy.^{4-6,20} Now, more than 40 years after the first contemporary description of HCM, it is perhaps timely to revisit and assess the true value of the ECG in the clinical evaluation of patients with this increasingly complex disease.

ECG AND MAGNITUDE OF HYPERTROPHY

Despite the instinctual expectation that the ECG in HCM depicts its diagnostic *cine qua non* of LV hypertrophy, analysis of large HCM populations report only weak (although statistically significant) correlations between the precordial and standard ECG lead voltages and the magnitude or distribution of LV hypertrophy (with coefficients in the range of only 0.3-0.4).¹⁷ LV hypertrophy patterns are present in only about one half of patients.⁹ Furthermore, there is little relationship between ECG voltages and the massive degrees of hypertrophy unique to a minority of HCM patients (i.e., with maximal wall thicknesses of 30 to 60 mm),^{7,21-24} or the magnitude of LV outflow tract obstruction due to mitral valve systolic anterior motion. Therefore, while ECG voltages may be

Address for reprints: Barry J. Maron, M.D., Minneapolis Heart Institute Foundation, 920 E. 28th Street, Suite 60, Minneapolis, MN 55407. Fax: 612-863-3875; E-mail: hcm.maron@mhif.org

striking, intuitively suggesting the presence of substantial LV hypertrophy and/or outflow obstruction in individual HCM patients, a consistent relationship between absolute thickness of the LV wall (or gradient) and the height or depth of R and S waves has not been documented.

In addition, there is little evidence of a clear link between ECG pattern and the precise distribution or location of LV wall thickening in HCM.^{9,17} For example, 25 years ago, Japanese investigators reported giant negative T waves to be a diagnostic marker for segmental hypertrophy involving the LV apex, a morphologic form of HCM that appears to be most common in that country.²⁵⁻²⁸ However, this association of a markedly inverted T-wave pattern and apical hypertrophy has been observed only occasionally in HCM patients outside of Japan.^{9,28} Also, the presence of pathologic Q waves are not pathognomonic for septal hypertrophy.⁹

ECG AND GENETIC DEFECTS

However, the application of molecular biology to HCM over the last decade,²⁻⁶ has strengthened the diagnostic value of the scalar ECG in this disease. For example, in selected family members identified as having a mutant disease-causing HCM gene by DNA laboratory analysis, or relatives in whom progression of hypertrophy was ultimately documented,^{20,31} the ECG may be abnormal *prior* to evidence of LV hypertrophy appearing on the two-dimensional echocardiogram.³² Therefore, ECG abnormalities alone may represent a marker for the presence of HCM. This situation is most frequently encountered in preadolescent children in their prehypertrophic phase,³² but also in some adult relatives exhibiting morphologic conversions much later in life (particularly when mutations in the myosin-binding protein C gene are responsible for HCM).⁵

Nevertheless, because routine laboratory DNA-testing is not yet readily accessible to the clinician, the patient without a family history of HCM presenting with an abnormal ECG and normal echocardiogram continues to represent a clinical dilemma. Recently, we have become convinced that magnetic resonance imaging possesses the diagnostic capability of identifying segmental LV hypertrophy undetectable by two-dimensional echocardiogram in patients suspected of having HCM.

ECG SCREENING

Because the vast majority of patients with HCM show one or more abnormalities on the ECG, this test has an important role in the screening of large general populations for HCM in which the echocardiogram is not deemed sufficiently cost-effective or practical as a primary diagnostic test. For example, in studies from Italy, where national population screening is mandated under certain circumstances, the ECG has proved efficacious in targeting individuals with unsuspected HCM during the preparticipation evaluations of young competitive athletes^{33,34} as well as military recruits.³⁵ In these clinical circumstances, the ECG will raise the clinical suspicion of HCM with the diagnosis ultimately confirmed by echocardiography.⁷

CONCLUSION

Although the 12-lead ECG may show striking abnormalities in many patients with HCM, it has not proved to be a reliable marker for the magnitude or pattern of LV hypertrophy in this disease, nor the presence of outflow obstruction. Alternatively, the ECG has recently demonstrated diagnostic value in a number of other clinical circumstances, such as the preparticipation screening of competitive athletes, and for the subsets of family members affected genetically by HCM, but prior to the phenotypic appearance of LV hypertrophy on echocardiogram. In this context, the scalar ECG continues to be a worthy complement for clinical evaluation of patients in the broad and complex HCM disease spectrum.

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