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REVIEWS

STATE-OF-THE-ART PAPERS

The Remarkable 50 Years of Imaging in HCM and How it Has Changed Diagnosis and Management

From M-Mode Echocardiography to CMR

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ABSTRACT

The almost 50-year odyssey of cardiac imaging in hypertrophic cardiomyopathy (HCM), revisited and described here, has been remarkable, particularly when viewed in the timeline of advances that occurred during a single generation of investigators. At each step along the way, from M-mode to 2-dimensional echocardiography to Doppler imaging, and finally over the last 10 years with the emergence of high-resolution tomographic cardiac magnetic resonance (CMR), evolution of the images generated by each new technology constituted a paradigm change over what was previously available. Together, these advances have transformed the noninvasive diagnosis and management of HCM in a number of important clinical respects. These changes include a more complete definition of the phenotype, resulting in more reliable clinical identification of patients and family members, defining mechanisms (and magnitude) of left ventricular outflow obstruction, and novel myocardial tissue characterization (including in vivo detection of fibrosis/scarring); notably, these advances afford more precise recognition of at-risk patients who are potential candidates for life-saving primary prevention defibrillator therapy. This evolution in imaging as applied to HCM has indelibly changed cardiovascular practice for this morphologically and clinically complex genetic disease. (J Am Coll Cardiol Img 2016;9:858–72)

Since the initial description of hypertrophic cardiomyopathy (HCM) >50 years ago, most of our understanding of this complex and heterogeneous genetic heart disease has resulted from insights gained through advances in cardiovascular imaging techniques. Indeed, perhaps no other heart disease has been so uniquely suited to noninvasive imaging as HCM (1–10). In many respects, the development of cardiac imaging from M-mode echocardiography to cardiac magnetic resonance (CMR) transpiring over several decades has paralleled the evolving understanding of this clinically and morphologically diverse disease (**Figures 1 and 2**). Therefore, in this comprehensive historical review, we revisit the development of imaging technology to assess its impact on the diagnosis and management of HCM (10).

THE BEGINNING

In the early 1960s, Dr. Harvey Feigenbaum (Indianapolis, Indiana) was largely responsible for the clinical adaptation of cardiac ultrasound (which he

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termed "echocardiography") (11–15), due to his vision, energy and focus, and fervent belief in this new technology. Dr. Feigenbaum formulated a worldwide initiative that included publications, workshops, national/international conferences, a comprehensive textbook spanning 45 years, the first commercially available sector scanner, and a cadre of trainees who carried forth a new message to a skeptical establishment.

Early investigations from the Feigenbaum laboratory reported the capability of measuring left ventricular (LV) wall thickness and cavity dimensions, and recognition of the ventricular septum (12,14–16). These observations and those of other investigators (17,18) were instrumental in promoting the imaging revolution for cardiac diseases (prominently including HCM).

EARLY HISTORICAL PERSPECTIVES ON CARDIAC/HCM DIAGNOSES

The initial contemporary morphologic description of HCM was recorded in 1958 by Dr. Donald Teare, the Coroner of London (19). In 8 young patients who had died suddenly, Dr. Teare described the classic gross and histologic features of HCM, including the asymmetric pattern of left ventricular hypertrophy (LVH) that ultimately became a diagnostic marker in the imaging era (20). Although these findings were considered possibly those of a cardiac tumor, his report is remarkable because it described for the first time, in novel anatomic detail, the disease entity that became HCM.

In the decade that followed (1960 to 1970), clinical recognition and investigation of HCM began in earnest, dominated by the Braunwald group at the National Institutes of Health (Bethesda, Maryland) (1). Their findings were largely hemodynamic and angiographic observations (**Central Illustration**) in the cardiac catheterization laboratory but also involved electrocardiograms, history-taking, and precordial auscultation. In 1958, a young man with a subaortic gradient and malignant family history became the first patient clinically diagnosed with HCM (21).

ECHOCARDIOGRAPHY AND M-MODE IMAGING. Introduction of echocardiography to clinical practice in the early 1970s signaled an abrupt transition from invasive cardiac catheterization to the modern imaging era (4,6,9,22,23) (**Central Illustration**). M-mode, a time-motion technique ("M" for motion), provided a single-dimensional ("ice pick") representation of the heart (3,11,12,22,23) directed blindly through narrow rib interspaces, dissecting the center of the LV cavity to avoid obliquity. Consequently, images of the LV wall were confined to a small portion of the basal anterior ventricular septum and posterior (inferior) LV free wall (**Figure 3**). Unlike 2-dimensional echocardiography (2DE), M-mode does not provide a true picture of the heart but rather a diagrammatic display showing changes in the position of structures during the cardiac cycle. Recordings were made initially on hard paper strips, or as Polaroid stop-frame snapshots.

In 1972, 2 HCM cohorts imaged with new M-mode technology were published in *Circulation* 3 months apart (one from the University of California at Los Angeles [22] and one from the National Institutes of Health [23]), quantitatively measuring LV wall thicknesses for the first time. This research represented a major milestone for HCM, providing the opportunity to achieve a reliable noninvasive diagnosis, while avoiding the risk and inconvenience of cardiac catheterization. In the process, a new era of clinical investigation was created (**Central Illustration**).

The asymmetrically hypertrophied ventricular septum was proposed as a diagnostic hallmark (20,23), and the capability for diagnosing HCM in the absence of a subaortic gradient was a major advance since obstruction was a diagnostic prerequisite in the decade before M-mode (1). This scenario is evident by the names used at that time: IHSS (idiopathic hypertrophic subaortic stenosis) and HOCM (hypertrophic obstructive cardiomyopathy) (24,25).

M-mode echocardiography made it possible to compare thicknesses of small portions of the ventricular septum and the LV free wall, and early National Institutes of Health investigators created the "septal-free wall ratio" (20,23). This ratio is usually abnormal in HCM because the anterior septum and posterior wall are generally the thickest and the thinnest portions of the LV chamber, respectively (**Figure 3**). Ratios ≥1.3 were initially promoted as pathognomonic diagnostic markers for HCM, leading to a brief renaming of the disease as "ASH" (asymmetric septal hypertrophy) (20). Unfortunately, characterizing a complex pathological process solely by using a single disease feature only added confusion, given the many acronyms already in use describing the same disease (24,25). Ultimately, the septal-free wall ratio proved to have low diagnostic specificity (26) and soon became obsolete as a HCM marker.

LV OUTFLOW OBSTRUCTION AND IMAGING. Surgical relief of LV outflow tract obstruction (1,2) began

ABBREVIATIONS AND ACRONYMS

2DE = 2-dimensional echocardiography

CMR = cardiac magnetic resonance

CT = computed tomography

LAMP = lysosome-associated membrane protein

LGE = late gadolinium enhancement

LV = left ventricular

LVH = left ventricular hypertrophy

SAM = systolic anterior motion