Evidence for Left Ventricular Outflow Tract Obstruction With Minimal Septal Hypertrophy

The Case Grows Stronger for a Multimodality Imaging Strategy for Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease caused by mutations in genes encoding proteins of the cardiac sarcomere and is associated with substantial heterogeneity in phenotypic expression and clinical course. Over the last 55 years, numerous advances have contributed enormously to our understanding of the diagnosis and treatment of patients with this disease. Throughout this continuum of progress, cardiovascular imaging has had a central role. Indeed, there is perhaps no other cardiovascular disorder more uniquely suited to noninvasive imaging than HCM, particularly given the enormous diversity in morphology, particularly with respect to the pattern and extent of left ventricular (LV) wall thickening and dynamic LV outflow obstruction.

However, the past 2 decades have witnessed a new era of imaging for this disease, with the emergence of cardiovascular MRI (CMR). This contemporary imaging technique provides 3-dimensional tomographic imaging, high spatial resolution, and sharp contrast between the blood pool and myocardium, unencumbered by some of the limitations of echocardiography, including obliquity of cross-sectional imaging planes.

For these reasons, CMR can be superior to echocardiography for HCM diagnosis by identifying areas of segmental hypertrophy (ie., anterolateral wall or apex) not reliably visualized by echocardiography (or underestimated in terms of extent). CMR has broadened our understanding of HCM expression to include phenotypic abnormalities which may not directly relate to sarcomere mutations, including abnormalities of the right ventricle, elongated mitral valve leaflets, papillary muscle architecture, accessory LV muscle bundles, and myocardial crypts.

In addition, new subgroups within the diverse HCM disease spectrum have emerged with CMR, including those with thin-walled scarred LV apical aneurysms (a subgroup largely unidentified before CMR), end-stage systolic dysfunction (EF <50%), and massive LV hypertrophy, raising consideration in these patients for additional management strategies, including implantable cardioverter-defibrillators and anticoagulation for stroke prophylaxis. More recently, contrast-enhanced CMR with late gadolinium enhancement has provided the opportunity to identify the abnormal myocardial substrate of fibrosis, with extensive fibrosis representing a novel marker for sudden death risk and thus creating the opportunity to more reliably identify patients for life-saving therapy with the implantable cardioverter-defibrillator.

For these reasons, the contemporary approach to diagnosis and management of HCM includes a complementary, multimodality strategy incorporating the unique imaging strengths of both echocardiography and CMR to improve treatment and outcome of patients with this complex genetic heart disease. This principle sets the stage for the study by Patel et al in this issue of Circulation: Cardiovascular Imaging, in which these imaging techniques were used to identify structural abnormalities of the mitral and subvalvular apparatus, which may be contributing to the development of LV outflow tract obstruction in an underappreciated subset of HCM patients with minimal LV hypertrophy (<18 mm). The majority of the HCM patients in this study had outflow tract gradients at rest or with provocation (≥30 mmHg), with one-third developing advanced limiting heart failure symptoms requiring surgery for relief of obstruction.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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Further Evidence for Multimodality Imaging in HCM

The authors assessed multiple echocardiographic views to measure anterior and posterior mitral valve leaflet length and identify abnormal chordal attachments to the mitral valve. With CMR, a detailed analysis of papillary muscles architecture was performed, including number, area, location, as well as extent of mobility (or laxity). These specific structural abnormalities of the LV outflow tract area were analyzed because they have previously been identified as being important contributors to the mechanism of outflow tract obstruction in HCM.11,16–20 For example, in HCM patients with substantially elongated mitral valve leaflets, the mitral–septal contact point (and site of subaortic obstruction) can be displaced distal to their usual position.16,18,19 In addition, apically displaced accessory anterolateral or extremely mobile double bifid papillary muscles can tether the plane of the mitral valve toward the ventricular septum facilitating the drag phenomenon of systolic anterior motion.16–20 Of note, as the authors point out,14 the analysis used in this study to quantify papillary muscle mobility is not standard and rather complex and potentially subject to significant variability, particular for centers without expertise in CMR imaging or HCM management. Therefore, whether this CMR analysis can be easily and reliably reproduced among the general cardiology community is uncertain.

In multivariable analysis, these morphological abnormalities were indeed identified as independent predictors for outflow obstruction, confirming similar findings from studies comprised of HCM patients with more extensive septal hypertrophy. These data do expand on these prior observations by incorporating multimodality imaging to provide a quantitative analysis for mitral valve and papillary muscles abnormalities. In particular, the tomographic high-resolution imaging capability of CMR is used to provide quantitative measures of these structures not possible with 2D echocardiography. Using a receiver operator curve analysis, cut-off values are provided for mitral valve leaflet length and papillary muscle mobility, which were predictive of outflow tract obstruction.

These data make several clinically relevant points. They substantiate that a diverse spectrum of morphological abnormalities of the mitral valve and subvalvular apparatus are present even among those HCM patients whose disease expression is otherwise limited to mild LV hypertrophy, expanding our appreciation for the heterogeneity of the HCM heart. This observation has led to an improved understanding of the complex mechanisms often responsible for developing outflow tract obstruction in HCM and is directly relevant to strategic planning for septal reduction procedures. In the past, myectomy has often not been considered a viable option for relief of obstruction in HCM patients with minimal basal hypertrophy because of perceived risk of complications, such as ventricular septal defect or suboptimal relief of obstruction, and thereby, mitral valve replacement has historically been the operative strategy of choice in these patients.1

However, in the current experience reported here, 45 HCM patients with minimal hypertrophy required surgical intervention for obstruction, with outflow gradients successfully eliminated and with no operative deaths reported within 30-days after surgery. The authors suggest that the high rate of successful relief of obstruction was a result of a great appreciation and understanding of the complex LV outflow tract anatomic abnormalities contributing to obstruction. For example, approximately half of the operated patients were identified as having structural abnormalities of the mitral valve or papillary muscles judged to be contributing to obstruction and requiring additional surgical interventions, including mitral valve repair/replacement and papillary muscle reorientation to completely eliminate obstruction. Based on these data, it is unlikely that a septal reduction approach with alcohol septal ablation would be effective at optimal relief of obstruction in this subset of obstructed HCM patients because the percutaneous procedure is inflexible with the operator confined to the fixed anatomic distribution of the first major septal perforator coronary artery and unable to address these concurrent structural abnormalities.1 Instead, surgical repair of these structural issues led to a reorientation of the mitral valve apparatus away from the ventricular septum and provided complete relief of obstruction without the need for resecting basal septal muscle. Presumably, if these morphological abnormalities of the LV outflow tract were not addressed as part of the surgical strategy, residual outflow obstruction may have contributed to incomplete resolution of limiting heart failure symptoms.3,16–19 Of note, 4 HCM patients (9%) required mitral valve replacement to ensure optimal resolution of gradient, a percentage for mechanical valve placement, which is greater than reported in other surgical series of myectomy patients,3,4 and therefore, HCM patients undergoing surgery for obstruction with minimal septal hypertrophy should be aware of this increased risk.

In this study, echocardiograms and CMRs were analyzed retrospectively and therefore not used to directly guide decision-making for invasive septal reduction therapies, nor were the imaging results used for presurgical planning in those patients who underwent myectomy for relief of obstruction. Decisions to repair the mitral valve or alter the papillary muscles were made intraoperatively, by the surgeon, under direct visualization of the LV outflow tract anatomy. Therefore, it remains unclear if the noninvasive detection of these structural abnormalities provides information which directly alters management strategies among the patients who are candidates for septal reduction therapy. For example, many of the abnormalities of the LV outflow tract were also present in HCM patients undergoing successful isolated myectomy. Nevertheless, these data by Patel et al14 provide a rationale and framework for the use of multimodality imaging in HCM to provide the surgeon anatomic information as part of preoperative planning. In this regard, additional studies are warranted in which results of multimodality imaging studies are discussed and integrated in a systematic, prospective fashion before invasive septal reduction procedures to clarify the impact on therapeutic decision-making and potential outcome.

In addition, longer-term follow-up of the surgical patients was not included as part of the current study design. Therefore, it is not clear whether the nonmyectomy surgical strategies performed in this study are durable over
extended periods of time, particularly relevant given the extensive repairs performed on the mitral valve, and whether compromise of the leaflets will result in significant mitral regurgitation during longer-term follow up, given the relatively youthful age at which surgery is performed in HCM patients.2,3,5 Also, this study was performed by experts in one of the largest HCM referral centers in North America, well known for its excellence and extensive experience in surgical myectomy.4 This is particularly relevant because the subgroup of HCM patients undergoing myectomy in this report are perhaps the most challenging surgical subgroup because of the limited basal hypertrophy, making potential risk for complications even greater. For this reason, it is unclear whether similar surgical results can be achieved in centers with less experience. Therefore, it seems prudent to provide patients the greatest opportunity for excellence to provide patients the greatest opportunity for surgical myectomy. Therefore, it seems prudent to report are perhaps the most challenging surgical subgroup for this reason, it is unclear whether similar surgical results can be achieved in centers with less experience. Therefore, it seems prudent to provide patients the greatest opportunity for excellence.

In conclusion, these data by Patel et al4 provide further evidence that we are indeed well into a new imaging era for HCM, in which a multimodality strategy incorporating the unique strengths of echocardiography and CMR improves diagnosis and alters management.2 These imaging techniques have been responsible for expanding our understanding of the incredibly diverse phenotypic expression of HCM, which has now been expanded to include the underappreciated subgroup of HCM patients with minimal LV hypertrophy but outflow tract obstruction. By applying a complementary imaging strategy to these patients, the mechanisms responsible for outflow obstruction can be identified ultimately, leading to appropriate treatment and successful relief of obstruction, thereby providing these HCM patients the opportunity to achieve a normal quality of life free of limiting heart failure symptoms.

Disclosures

None.

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