Deformation imaging in Hypertrophic Cardiomyopathy: Fact or fiction?

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Marc Vivien Foe of Cameroon is taken off the field during a semifinal Confederations Cup match on June 26, 2003. He died that night, with an autopsy later revealing HCM.
However, the hypertrophic phenotype is a common final pathway of multiple different genetic and acquired conditions, including abnormal load conditions, sarcomeric abnormalities (hyperplasia, hypertrophy, and disarray), and intracellular and interstitial accumulation of different materials (Amyloid, fibrosis, infiltration, etc).

**Sarcomeric HCM** results from mutations in genes encoding sarcomeric proteins, transmitted in an autosomal dominant inherited pattern, with incomplete penetrance and variable expression.

>1400 mutations in 13 cardiac sarcomere & myofilament-related genes are identified.
Demonstrates cardiac morphology

Extent of SAM of the MV

Diastolic Function

Degree of MR

Severity of LVOT gradient

Conventional Echo in HCM

Transthoracic echocardiography evaluation in hypertrophic cardiomyopathy

Recommendations

In all patients with HCM at initial evaluation, transthoracic 2-D and Doppler echocardiography are recommended, at rest and during Valsalva manoeuvre in the sitting and semi-supine positions—and then on standing if no gradient is provoked.

Measurement of maximum diastolic wall thickness is recommended, using 2-D short-axis views in all LV segments, from base to apex.

A comprehensive evaluation of LV diastolic function is recommended, including pulsed Doppler of mitral valve inflow, tissue Doppler velocities at the mitral annulus, pulmonary vein flow velocities, pulmonary artery systolic pressure, and measurement of LA size and volume.

In symptomatic patients with a resting or provoked peak instantaneous LV outflow tract gradient <50 mm Hg, 2-D and Doppler echocardiography during exercise in the standing, sitting or semi-supine position is recommended to detect provokable LVOTO and exercise induced mitral regurgitation.
Is conventional echo sufficient for such complex disease?

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**Table 1: Echocardiographic pitfalls**

**Conventional echocardiographic pitfalls**

- False positive diagnosis of HCM
  - Conditions simulating LVH/ASH
    - Oblique sections of ventricular walls (off-axis views)
    - Moderator band (right ventricular)
    - Left ventricular false tendons
    - Sigmoid septum of elderly
  - Other forms of ventricular hypertrophy
    - Hypertensive patients with inferior myocardial infarction
    - Right ventricular hypertrophy
    - Athlete’s heart
    - Infiltrative disorders
    - Cardiac amyloidosis
    - Haemochromatosis
    - Friedreich’s ataxia
    - Incidental detection of outflow tract gradient
    - Associated with ventricular hypertrophy
    - Dialysis patients

- False negative diagnosis of HCM
  - Conditions without ASH
    - Apical hypertrophy
    - Localised LVH
    - Mild concentric LVH
  - Absence of left ventricular hypertrophy
    - Children and adolescents
    - Protein binding C mutations
    - Troponin T mutations
    - End stage HCM with dilated fibrotic LV
Why conventional echo is not sufficient?

- Unfortunately, because of molecular heterogeneity and the limited number of genotyped families, genetic analysis have proved disappointing.

- Mutations in genes encoding sarcomeric proteins are not found in up to one third of patients with HCM and the diagnosis remains a clinical rather than a ‘genetic’.

- So more sophisticated techniques are required for disease characterization.
The epicardial fibers course obliquely toward the apex & endocardial fibers course obliqueley toward the base. The special architecture results in complex 3D deformation process. The apex stays relatively stationary, while the base of the heart moving downwards for blood ejection.

In the heart sample from the patient with HCM, myocardial disarray, abnormal branching, and bizarre myocardial hypertrophy (B, C) (increased interstitial connective tissue elements).

An Ultrasound Speckle Tracking (Two-Dimensional Strain) Analysis of Myocardial Deformation in Professional Soccer Players Compared With Healthy Subjects and Hypertrophic Cardiomyopathy

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**CLINICAL INVESTIGATIONS**

**HYPERTROPHIC CARDIOMYOPATHY**

Systolic Myocardial Mechanics in Hypertrophic Cardiomyopathy: Novel Concepts and Implications for Clinical Status

Sherry Carasso, MD, Hau Yang, MD, Anna Wong, MD, FACC, Masri A. Vaknis, MD, FACC, Michel Janosi, MD, FACC, E. Doughty Wight, MD, FACC, and Harry Hakowski, MD, FACC, FPCPC, FASE, Toronto, Ontario, Canada, and Irvine, California

In hypertrophic cardiomyopathy (HCM), malfunctioning sarcomeric protein, myocyte hypertrophy, fibrotic disarray, and interstitial fibrosis interfere with systolic myocardial mechanics despite clinically-hypodynamic systolic function. We evaluated local left ventricular (LV) mechanics in 72 patients with HCM and 32 control subjects using 2-dimensional velocity vector imaging. Patients had higher circumferential strain (−34 ± 9 vs −29 ± 8, P < .05) and lower longitudinal strain (−16 ± 4 vs −21 ± 4, P < .05) compared with control subjects. Biphasic strain vector magnitude was similar (−38% vs −36 ± 7) in both groups, but was circumferentially oriented in HCM (27 ± 10 vs 36 ± 3 degrees, P < .05). MdLV rotation was clockwise (opposite to normal). LV outflow tract obstruction and clinical status was related to more circumferentially directed strain and reduced apical biventricular strain. Patients with HCM have more circumferential myocardial strain and apically displaced systolic fold. Functional status and LV outflow tract obstruction were related to decreased strain vector angle and apical mechanics. These findings provide insights into the pathophysiology of HCM.

Key words: Hypertrophic cardiomyopathy, Mechanics, Strain, Echocardiography, Tissue tracking

Hyperkrophic cardiomyopathy (HCM) is a primary disorder of the myocardium caused by mutations in cardiac sarcomeric protein. Histopathologically it is associated with myocardial hypertrophy, fiber disarray, increased loose connective tissue, and predominantly circumferential orientation, whereas epicardial fibers course obliquely toward the apex, and endocardial fibers course obliquely toward the base. This creates twist of the LV during contraction while maintaining uniform transmural distri...
Longitudinal systolic strain is significantly lower in patients with HCM compared with control subjects. Carasso et al. JASE, 2008

- LV twist is apicaly displaced. This may be consistent with the hypertrophied and rigid myocardium of HCM, which prevents a more gradual change of rotation from base to the apex.

Carasso et al. JASE, 2008
HCM versus Hypertension...

Strain criteria

HCM

Hypertension

Badran et al. (J Am Soc Echocardiogr 2013;26:1397-406)
Results:

\[ L_{sys}, SR_{sys}, E_{sys}, \text{ and } A_{sys} \text{ were significantly lower, at rest } \& \text{ EX. } \& \text{ more dyssynchrony vs HTN.} \]

\[ \text{Circumferential } \varepsilon_{sys} \text{ and twist were higher, compared with HTN and controls (} P < .0001\).} \]

Exercise capacity was clearly correlated with systolic functional reserve.

Conclusion

- The direct relationship between abnormal systolic functional reserve and exercise capacity in HCM population, suggesting its imp. in determination of clinical status even with normal EF.
Global and Regional Myocardial Function Quantification by Two-Dimensional Strain: Application in Hypertrophic Cardiomyopathy

- 26 familial non-obstructive HCM.
- 15 (57.7%) had asymmetrical & 11 (42.3%) concentric HCM.
- 45 healthy subjects
- The LV is divided into 17 segments and examined with 2D strain.

-Longitudinal, transverse strains, Circumferential and radial strains are analyzed.
15 (57.7%) had asymmetrical & 11 (42.3%) concentric HCM.

In asymmetric HCM, longitudinal strain is significantly higher while circumfrential strain is lower versus concentric HCM $P<0.05$.

Serri et al. JACC : 2006 Vol. 47, No. 6,
Abnormal Strain Patterns

2D (top panels) and bull’s eye plots (bottom panels) show (A) an apical sparing pattern in cardiac amyloidosis and (B) abnormal septal strain in hypertrophic cardiomyopathy; (C) reduced apical strain in apical variant hypertrophic cardiomyopathy; and (D) again a reduced apical strain in apical infarction.

What is clinical significance of deformation abnormalities?
Regional peak LS by speckle tracking provides useful information noninvasively to distinguish fibrotic from non-fibrotic lesions in LVM in HCM subjects using CMR.

Horie et al, Circulation.2012; 126: A17166

Results: Regional peak LS absolute values were significantly lower in fibrotic-lesions than in non-fibrotic lesions (-8.9±5.6%, and -11.3±5.9%, respectively, P<0.001).

Methods: 2D strain was applied to assess LS and compared it with development of NSVT in Holter monitoring,

Results: NSVT on Holter monitoring was correlated to LS while no significant associations between & LV outflow gradient, LA diameter, E/Em or LV ejection fraction.

Mid septal strain >–10.5% had a sensitivity of 89% and a specificity of 74% for predicting NSVT independently of age or MWT.
Genetic conditions that are not caused by cardiac sarcomere mutations & associated with severe LVH and usually coupled Multi-system affection

These conditions include a variety of disorders: glycogen storage disorders, lysosomal storage disorders, mitochondrial cytopathies, cardiac amyloidosis and disorders of fatty acid metabolism.

They differ significantly from HCM due to sarcomeric mutations in terms not only of pathogenesis of hypertrophy but also of clinical features and prognosis.
Grey zone: new echo criteria

HCM versus physiologic hypertrophy ...

Athletes' HCM

Am J Cardiol 2007

An Ultrasound Speckle Tracking (Two-Dimensional Strain) Analysis of Myocardial Deformation in Professional Soccer Players Compared With Healthy Subjects and Hypertrophic Cardiomyopathy

Viviane Richard, MD, Stéphane Lafitte, MD, PhD, Patricia Reant, MD, Karim Serri, MD, Marianne Lafitte, MD, Stephanie Brette, MD, Akem Kerouani, PhD, Hakim Chalabi, MD, Pierre Dos Santos, MD, PhD, Herve Douard, MD, and Raymond Roudaut, MD

Deformation analysis using 2-dimensional strain echocardiography can detect early systolic function abnormalities in patients with left ventricular hypertrophy. This study was designed to characterize global and regional myocardial deformation using 2-dimensional strain in professional soccer players (PSPs) compared with control subjects and patients with hypertrophic cardiomyopathy (HC). Twenty-nine PSPs, 26 patients with HC, and 17 controls were investigated at rest using transthoracic echocardiography with 2-dimensional strain analysis. Radial and transverse strains were significantly higher in PSPs compared with controls, whereas longitudinal strain was lower. Compared with patients with HC, athletes had higher values for transverse, radial, and circumferential strains. In pathologic hypertrophic segments, longitudinal strain was lower in patients with HC than in PSPs. In conclusion, 2-dimensional strain can identify specific patterns of myocardial deformation in PSPs, controls, and patients with HC. It has the potential to become a routinely used method for the differentiation of athlete's heart and HC. © 2007 Elsevier Inc. All rights reserved. (Am J Cardiol 2007;100:128–132)
Longitudinal strain is lower in HCM compared with PSPs in the septal and anterior walls, particularly in basal and mid-inferoseptal LV segments. A cutoff of -11% in basal and -13% in mid-septal longitudinal strain specificity of 77% and sensitivity of 73%.)

Take Home Message

- With the use of deformation imaging, it is now possible to spatially map & identify regional heterogeneity in contractile function in HCM with an important advance in our understanding of deranged myocardial mechanics.

- Longitudinal deformation is the most vulnerable component of LV mechanics & it is linked to the more fibrotic areas and correlated to exercise capacity and development of arrhythmias in this complex disease.