Right Ventricular Remodeling, Its Correlates, and Its Clinical Impact in Hypertrophic Cardiomyopathy

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Background: Structural right ventricular (RV) abnormalities are present in a substantial proportion of patients with hypertrophic cardiomyopathy (HCM), but the trigger for RV hypertrophy remains unclear. The aim of this study was to assess the relationship between RV and left ventricular (LV) remodeling and the impact of biventricular involvement on clinical status in this setting.

Methods: Ninety-nine patients with HCM and 30 normal subjects with a similar age and gender distribution were prospectively enrolled. Comprehensive echocardiography was performed in all, including the assessment of LV and RV function by tissue Doppler and speckle-tracking echocardiography. Measurement of RV free wall thickness (RVWT) was performed at end-diastole, in a zoomed subcostal view, focusing on the RV midwall.

Results: Patients with HCM had increased RVWT (6.4 ± 1.9 vs 3.6 ± 0.8 mm, $P < .001$) and lower values of RV global longitudinal strain (−19.4 ± 4.4% vs −23.8 ± 2.7%, $P < .001$) compared with control subjects. RVWT was independently related to LV mass and LV global longitudinal strain. Increased RVWT was correlated with New York Heart Association class ($r = 0.20$, $P = .04$) and calculated sudden cardiac death risk score ($r = 0.52$, $P < .001$) and was independently related to the presence of ventricular arrhythmias (odds ratio, 2.02; 95% CI, 1.28–3.19; $P = .002$).

Conclusions: In patients with HCM, the presence of RV hypertrophy was associated with increased LV mass and reduced LV longitudinal strain, correlated with increased calculated sudden cardiac death risk score, and independently related to the presence of ventricular arrhythmias. These data suggest more severe disease in patients with biventricular HCM. (J Am Soc Echocardiogr 2015;■:■-■.)

Keywords: Hypertrophic cardiomyopathy, Right ventricle, Right ventricle remodeling, Speckle-tracking echocardiography, Ventricular arrhythmia

Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease, characterized by great morphologic, functional, and clinical heterogeneity. Myocardial hypertrophy, the classical phenotypic hallmark of this condition, can be found at any location, including the right ventricle.[1] Structural right ventricular (RV) abnormalities, present in a substantial proportion of patients with HCM,[2] can be a consequence of the sarcomeric protein genetic mutations, afterload changes, or ventricular interdependence, but the main trigger remains unclear. Few data are presently available about the relationship between left- and right-heart remodeling in this setting.[2,3]

In a close interdependence with morphologic changes, RV dysfunction can be an important marker of RV involvement in the myopathic process that characterizes HCM. However, because of the right ventricle's complex shape and high load dependency, the accurate and reproducible assessment of RV function is still difficult, and the available data are limited. Several studies performed in patients with HCM have demonstrated RV diastolic[4] and systolic[5] dysfunction, as assessed by conventional parameters such as tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (FAC), and RV myocardial performance index. On the other hand, the assessment of myocardial deformation by two-dimensional

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Abbreviations

CMR = Cardiac magnetic resonance

ECG = Electrocardiographic

FAC = Fractional area change

GLS = Global longitudinal peak systolic strain

HCM = Hypertrophic cardiomyopathy

ICD = Implantable cardioverter-defibrillator

LA = Left atrial

LV = Left ventricular

LVWT = Left ventricular wall thickness

NSVT = Nonsustained ventricular tachycardia

NYHA = New York Heart Association

RV = Right ventricular

RVH = Right ventricular hypertrophy

RVWε = Longitudinal strain of the right ventricular free wall

RVWT = Right ventricular free wall thickness

SCD = Sudden cardiac death

sPAP = Systolic pulmonary artery pressure

STE = Speckle-tracking echocardiography

TAPSE = Tricuspid annular plane systolic excursion

2D = Two-dimensional

(2D) speckle-tracking echocardiography (STE) could provide a more accurate quantification of regional RV function and potentially additional information on clinical impact in this setting.[6]

Changes in the morphology, structure, and function of the myocardium are responsible for the main clinical features of this disease: heart failure and arrhythmias. Although a large body of evidence supports the impact of left ventricular (LV) remodeling on the clinical status, there are few data regarding the relationship between RV remodeling and the clinical expression of the disease.[2,7]

We hypothesized that in patients with HCM, (1) RV remodeling is a frequent finding, closely interrelated with LV remodeling, and (2) heart failure symptoms and arrhythmias are related to RV remodeling.

METHODS

Study Population

We prospectively screened for enrollment 166 consecutive patients referred to our echocardiography laboratory between April 2009 and February 2015 who met the diagnostic criteria for HCM: M-mode and 2D echocardiographic evidence of wall thickness ≥ 15 mm in one or more LV myocardial segments in the absence of exercise training history and of cardiac or systemic conditions capable of inducing that magnitude of hypertrophy.[1] Patients with concomitant hypertension were included in the study population only if they had clear features favoring the diagnosis of HCM: family history of HCM, RVH, maximal LV wall thickness (LVWT) ≥ 15 mm, severe LV diastolic dysfunction, or marked repolarization abnormalities on electrocardiography.[1]

Patients with poor acoustic window ($n = 10$), those who were technically unsuitable for Speckle-tracking echocardiographic analysis ($n = 10$), and those with nonsinus rhythm ($n = 20$ patients with atrial fibrillation and $n = 4$ patients with atrial flutter), valvular prostheses ($n = 4$), pacemakers ($n = 8$), LV segmental wall motion abnormalities ($n = 3$), endocarditis ($n = 2$), and suspected amyloidosis ($n = 6$) were excluded.

Patients suspected on the basis of common clinical and laboratory data (electrocardiography, standard biology) of having causes of LV hypertrophy other than sarcomeric gene mutation and those with significant valvular heart disease other than mitral regurgitation were not eligible.

The final study population consisted of 99 patients.

Thirty healthy volunteers with a similar age and gender distribution served as a control group. They had no evidence of heart disease by physical examination, 12-lead electrocardiography, and echocardiography, and they were taking no medications. All subjects gave informed consent to participate in the study.

Clinical Data

The following clinical data were collected: age, gender, history of smoking, hypertension (defined as a history of hypertension requiring medical therapy), diabetes mellitus, and hypercholesterolemia. A family history of HCM or sudden death and the presence of chest pain, dyspnea, or syncope were also assessed. Clinical status was defined according to the New York Heart Association (NYHA) functional classification. In 91 of the 99 patients, 24-hour ambulatory electrocardiographic (ECG) monitoring using a Schiller-type Holter monitor was performed within 1 month of the echocardiographic study. The following arrhythmias were assessed: ventricular tachycardia (defined as three or more consecutive ventricular premature beats at a rate of ≥120 beats/min) and paroxysmal atrial fibrillation (defined as at least one period of >30 sec in duration of an absolute arrhythmia without detectable P waves and without a pattern consistent with an alternative diagnosis). The 5-year risk for sudden cardiac death (SCD) was estimated using the HCM Risk-SCD model.[1] Routine laboratory testing, including renal function testing, was performed in 90 hospitalized patients. Information regarding current medications was also obtained.

Echocardiography

A commercially available ultrasound machine (Vivid 7 or Vivid E9, GE Vingmed Ultrasound AS, Horten, Norway) equipped with an M4S probe was used for all echocardiographic examinations. Standard echocardiographic views were obtained using second-harmonic imaging with frequency, depth, and sector width adjusted for frame-rate optimization (60–100 frames/sec). Image settings and frame rates were kept similar for LV four-chamber, two-chamber, and long-axis apical views, which were recorded immediately one after another.[8] LV diameters, the thicknesses of the interventricular septum and LV posterior wall, and left atrial (LA) anteroposterior diameter were measured according to guideline recommendations.[9] The maximal diastolic LVWT was measured, using 2D short-axis views in all LV segments, from base to apex.[1] LV volumes and ejection fraction were calculated using the Simpson biplane method.[9] LV mass was calculated using the equation of Devereux.[10] All volumes and LV mass were normalized to body surface area. Basal RV diameter and minor axis of the right atrium were measured in the apical four-chamber view. The RV wall was visualized from different echocardiographic views (Figure 1) and was carefully assessed in motion in order to identify the maximal wall thickness, excluding epicardial fat or ventricular trabeculae. Measurement of RV free wall thickness (RVWT) was performed at end-diastole, below the tricuspid annulus at a distance approximating the length of the anterior tricuspid leaflet when it is fully open, in a zoomed subcostal view with focus on the RV midwall.[9,11,12] In patients with inadequate subcostal windows, measurement was performed in left parasternal windows. RVWT > 5 mm was used to define the presence of RVH.[9,11,12] TAPSE was measured as an index of longitudinal systolic RV