J Chin Med Assoc

ORIGINAL ARTICLE

Risk stratification in patients with hypertrophic cardiomyopathy: Looking beyond the left side myocardial function

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Abstract

Background: Patients with hypertrophic cardiomyopathy (HCM) have heterogeneous outcomes. As risk stratification mostly focuses on left-side myocardial function, we sought to investigate the prognostic value of right ventricular (RV) function in patients with HCM.

Methods: This retrospective cohort study included patients with HCM. Conventional ventricular functional parameters, including left ventricular ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), and fractional area change were obtained. The longitudinal strain was analyzed using the speckle tracking method. The primary endpoint was defined as a composite of hospitalization for heart failure, sustained ventricular tachycardia, or all-cause death.

Results: A total of 56 patients with HCM (aged 58.0 ± 14.9 years, 64.3% male) were included. After a mean follow-up duration of 30.1 ± 17.4 months, primary endpoints developed in 10 (20%) of 50 patients who were treated medically. Patients with cardiovascular events had a more reduced LV thickest segmental strain, worse TAPSE, and more impaired RV free wall strain. After adjusting for age, sex, and LVEF, TAPSE (hazard ratio [HR], 95% confidence intervals [CIs]: 0.24, 0.06-0.93) and RV free wall strain (HR, 95% CIs:1.12, 1.03-1.21) remained independent prognostic predictors. Incorporating either TAPSE or RV free wall strain provides incremental prognostic value to the LV strain alone (net reclassification improvement by 31.4% and 34.1%, respectively, both $p < 0.05$).

Conclusion: RV function assessed by TAPSE or RV free wall strain is predictive of subsequent cardiac events, suggesting that a comprehensive evaluation of RV function is useful for risk stratification in patients with HCM.

Keywords: Hypertrophic cardiomyopathy; Longitudinal strain; Right ventricular function; Risk stratification; Speckle tracking echocardiography

1. INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a common inherited disorder defined as marked left ventricular hypertrophy (LVH) in the absence of secondary causes.[1,2] HCM is characterized by diverse phenotypes ranging from being asymptomatic to progressive heart failure (HF), recurrent arrhythmia, or sudden cardiac death (SCD).[3] In view of the significant strides over the past decade, risk stratification in HCM has identified major risk factors for SCD.[1] Although the risk factors vary between guidelines, cardiovascular imaging has played a pivotal role to facilitate clinical decision making.[4] However, predictors for other HCM-related complications have not been comprehensively investigated. In addition, as parameters used for risk stratification are mostly derived from the left-sided chambers,[5,6] little is known about the prognostic value of the right ventricular (RV) indices.

The RV is susceptible to increased filling pressure transmitted from the hypertrophied left ventricle (LV). Previous studies showed that impaired RV systolic function was significantly associated with reduced functional capacity in patients with HCM and was correlated with poorer LV systolic function.[7,8] McKenna et al demonstrated that increased RV wall thickness is predictive of an increased incidence of arrhythmia and dyspnea.[9,10] However, as conventional echocardiographic parameters fail to detect subclinical RV myocardial deformation in an earlier

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Author Contributions: Dr. Hao-Chih Chang and Dr. Hao-Min Cheng contributed equally to this work.

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2023) 86: 19-25.

Received June 14, 2022; accepted September 2, 2022.

doi: 10.1097/JCMA.0000000000000825.

stage,[11] it has been reported that reduced RV myocardial strain can be detected before the change in RV ejection fraction (EF).[12] Since most patients with HCM exhibit preserved RV function by conventional parameters, we hypothesize that speckle tracking echocardiography (STE) can be of added significance for risk stratification among patients with HCM. Thus, this study aimed to determine the prognostic value of echocardiographic indices for assessing RV function, including STE measurements, in patients with HCM.

2. METHODS

2.1. Study participants

We conducted a retrospective cohort study enrolling patients aged ≥20 years with a hypertrophic LV who were referred to Taipei Veterans General Hospital between September 2016 and March 2019. The clinical diagnosis of HCM was established by experienced cardiologists based on echocardiography or cardiovascular magnetic resonance (CMR) imaging showing unexplained LVH with an end-diastolic wall thickness of >15 mm in the absence of other secondary causes, including systemic hypertension, valvular or subvalvular aortic stenosis, or infiltrative cardiomyopathy, such as amyloidosis, Anderson-Fabry disease, or glycogen storage disease. Baseline characteristics, including body mass index, smoking status, history of syncope, family history of SCD, and 6-minute walk distance, were recorded. The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease equation.[13] This study was approved by the Institutional Review Board of Taipei Veterans General Hospital and conformed to the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from each patient.

2.2. Transthoracic echocardiography

Comprehensive transthoracic echocardiography was conducted using a Toshiba Artida ultrasound machine with a 2.5 MHz phased-array transducer. All measurements were performed in accordance with the recommendations of the American Society of Echocardiography.[14]

2.2.1. Conventional measurements

The thickness of the interventricular septum was measured using M-mode at end-diastole. Left ventricular ejection fraction (LVEF) was determined using the bi-plane Simpson's method. Left atrial (LA) volume and LV mass were measured in the apical four-chamber view using the area-length method and were further divided by body surface area to calculate LA volume index and LV mass index, respectively. The LV morphological pattern was determined as previously described.[15] Maximal LV wall thickness was measured at end-diastole, and the LV segment with the maximal wall thickness was determined according to the American Heart Association consensus.[16] Transmitral inflow parameters including peak of early (E) and late (A) diastolic filling velocities were measured using pulsed wave Doppler, whereas early diastolic (e′) mitral annulus velocity was measured using tissue Doppler. Left ventricular outflow tract (LVOT) peak pressure gradients were measured in apical views using continuous-wave Doppler. LVOT obstruction was defined as a peak instantaneous outflow gradient estimated to be greater than 30 mmHg. RV free wall thickness was measured at end-diastole from the subcostal view at the level of the tip of the anterior tricuspid leaflet.[17] Right ventricular systolic pressure (RVSP) was estimated using Doppler echocardiography by calculating the trans-tricuspid pressure gradient during systole and the right atrial pressure by the dimension and collapsibility of the inferior vena cava. Tricuspid annular plane systolic excursion (TAPSE) was measured at the tricuspid lateral annulus as the displacement of systolic RV excursion by M-mode. The RV end-diastolic and end-systolic areas were obtained from the apical four-chamber view. The RV fractional area change (FAC) was calculated as the difference between the end-diastolic and end-systolic areas divided by the end-diastolic area.

2.2.2. Speckle tracking analysis

All images were analyzed using a two-dimensional speckle tracking method using TOMTEC Imaging Arena Cardiac Performance Analysis, Version 4.6 (TOMTEC, Unterschleissheim, Germany). All measurements complied with the joint consensus for the standardization of LV and RV deformation imaging using two-dimensional STE.[18,19] Briefly, after manual tracing of the endocardial border at the end-systolic frame, a region of interest was automatically generated with further manual adjustment. LV longitudinal strain was analyzed from apical two-, three-, and four-chamber views. Peak systolic strain was measured in each LV segment and averaged to calculate global longitudinal strain (GLS). The LV segmental longitudinal strain of the thickest LV segment was determined as the thickest segmental strain of the LV. RV strain was analyzed using an RV-focused apical four-chamber view. The RV free wall strain was calculated as the mean of the basal, mid, and apical segments of the RV free wall, whereas the RV septal strain was calculated as the mean of the basal, mid, and apical segments of the interventricular septum (Fig. 1). Poorly tracking segments or images that could not be optimized were excluded from the analysis. In patients with atrial fibrillation, we measured the strain from at least three consecutive cardiac cycles and the measurements were averaged.[20] For the reliability of the measurements, speckle tracking analysis was performed by another experienced and double-blinded observer (D.Y.L.). Interobserver variability was estimated in 20 randomly selected subjects by a second observer who was blinded to the first observer's measurements.

2.3. Follow-up and clinical outcomes

The primary endpoint was prespecified as a composite of the common complications of HCM, including hospitalization for HF, ventricular tachycardia, or all-cause mortality. Hospitalization for HF was based on the clinical presentation of typical HF signs and symptoms, chest radiography, and elevated N-terminal pro B-type natriuretic peptide. Sustained ventricular tachycardia was defined as consecutive ventricular beats at a rate of ≥100 beats per minute lasting more than 30 seconds as recorded by Holter monitoring, the necessity to receive catheter ablation, or implantable cardioverter defibrillator implantation. All participants were followed up regularly at outpatient clinics in the third and sixth months and then annually to ascertain any development of adverse events.

2.4. Statistical analyses

Continuous variables are presented as mean ± standard deviation and were compared using Student's t-test or analysis of variance. Categorical variables are expressed as frequencies (percentages) and compared using the chi-square test. Pearson's correlation coefficient was used to evaluate the association between RV strain and left-sided echocardiographic parameters. Estimations of the predictors of the primary endpoints were performed using Cox proportional hazard models. Hazard ratios (HR) and 95% confidence intervals (CIs) were calculated as relative risk estimates. The parameters of univariate significance were further adjusted in the multivariable models. To determine the optimal cutoff value for detecting increased risk for the primary endpoints, receiver operating characteristic (ROC) curve analysis was used. Kaplan–Meier survival curve analysis was used to

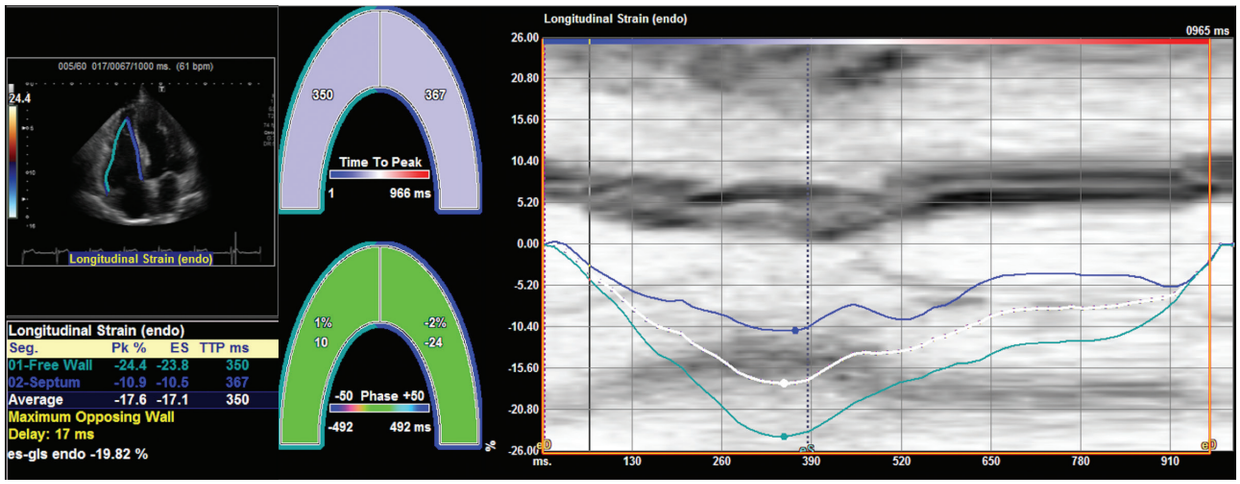

Fig. 1 Schematic demonstration of the measurement of right ventricular longitudinal strain using the TOMTEC Imaging System.

Table 1

Demographic and clinical characteristics of the study cohort

Variables	Values
Age (years)	58.0 ± 14.9
Male, n (%)	36 (64.3)
BMI (kg/m^2)	25.5 ± 3.7
Six-minute walk distance (m)	470.4 ± 130.0
eGFR (ml/min/1.73m^2)	75.7 ± 18.7
SBP (mmHg)	121.4 ± 15.7
DBP (mmHg)	67.9 ± 13.0
Comorbidities, n (%)	
Hypertension	26 (46.4)
Diabetes	3 (5.4)
Atrial fibrillation	11 (19.6)
Heart failure	8 (14.3)
Subtypes, n (%)	
Septal hypertrophy	45 (80.4)
Diffuse hypertrophy	5 (8.9)
Mid-ventricular hypertrophy	3 (5.4)
Apical hypertrophy	3 (5.4)
Plain measurements	
LA volume index (mm)	39.2 ± 7.8
LV maximal wall thickness (mm)	17.9 ± 4.8
LV mass index (g/m^2)	147.7 ± 39.0
LVOT obstruction, n (%)	18 (32.1)
LVEF (%)	76.3 ± 10.9
E/e′	13.3 ± 9.3
RVSP (mmHg)	28.0 ± 15.4
RV-free wall thickness (mm)	10.0 ± 2.2
TAPSE (cm)	2.5 ± 0.6
RV FAC (%)	36.4 ± 14.4
Strain measurements	
LV GLS (%)	−13.3 ± 3.1
LV thickest segmental strain (%)	−10.0 ± 7.6
RV free wall strain (%)	−18.6 ± 8.2
RV septum strain (%)	−8.5 ± 4.8

BMI = body mass index; eGFR = estimated glomerular filtration rate; FAC = fractional area change; IVS = interventricular septum; LA = left atrium; LV = left ventricle; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; RV = right ventricle; RVSP = right ventricular systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

assess prognostic significance stratified by different RV function parameters. The incremental prognostic value of RV function was evaluated using ROC curve analysis and net reclassification improvement (NRI). Interobserver variability was assessed using the intraclass correlation coefficient (ICC).[21] All statistical analyses were performed using SPSS version 24.0, MedCalc Version 19.0.4, and SAS version 9.4. All tests were two-sided, and a *p*-value of <0.05 was considered statistically significant.

3. RESULTS

3.1. Baseline characteristics

We enrolled a total of 56 HCM patients, with a mean age of 58.0 ± 14.9 years and 64.3% men. More than half of the patients had septal hypertrophy (80.4%), followed by diffuse hypertrophy (8.9%), mid-ventricular hypertrophy with apical aneurysm (5.4%), and apical hypertrophy (5.4%). All participants had preserved LV systolic function (LVEF ≥ 50%). The mean LV maximal wall thickness was 17.9 ± 4.8 mm. The patients' clinical and echocardiographic characteristics are presented in Table 1.

The clinical characteristics according to tertiles of RV GLS are shown in Table S1, http://links.lww.com/JCMA/A163. Compared to patients in the lower tertile, those in the upper tertile had a greater reduction in LV GLS, RV free wall, and septal strain. In contrast, LA and LV size, LV mass index, LVEF, E/e′ ratio, percentage of LVOT obstruction, RVSP, and RV free wall thickness were similar among the three groups. Table S2, http://links.lww.com/JCMA/A163 shows the associations between RV septal or free wall strains and left-sided chamber parameters. Significant associations were observed between RV free wall strain and LV strains but not between RV septal and LV strains.

3.2. Follow-up and survival analysis

Of all the enrolled patients, 50 (89.3%) patients who were managed medically and did not require non-pharmacological interventions (eg, alcohol septal ablation, surgical myomectomy, pacemaker, or implantable cardioverter defibrillator implantation) were included in the survival analysis. Over a mean follow-up duration of 30.1 ± 17.4 months, 10 (20%) patients developed primary endpoints, including four HF hospitalizations, four ventricular tachycardias, and two deaths. Patients with cardiovascular events during follow-up were older, tolerated a shorter 6-minute walk distance, had a larger LA volume index, larger LV mass index, lower LVEF, higher E/e′ ratio, smaller TAPSE and RV FAC, and reduced LV thickest segmental strain and RV free wall strain (Table 2). In the univariate Cox regression

Table 2

Comparison of clinical and echocardiographic parameters between medically treated patients with and without composite events

Variables	Events (–) (n = 40)	Events (+) (n = 10)	*p*
Age (years)	55.3 ± 15.3	65.9 ± 8.9	0.041
Male, n (%)	28 (87.5)	4 (40)	0.077
BMI (kg/m^2)	25.5 ± 3.3	25.4 ± 5.8	0.942
6-minute walk distance (m)	529.8 ± 78.1	408.5 ± 103.8	0.005
eGFR (ml/min/1.73m^2)	78.8 ± 18.7	64.7 ± 19.2	0.040
Plain measurements			
LA volume index (ml/m^2)	31.9 ± 16.4	47.7 ± 15.4	0.008
LV maximal wall thickness (mm)	17.8 ± 5.0	19.2 ± 3.9	0.455
LV mass index (g/m^2)	146.5 ± 50.8	193.3 ± 30.5	0.012
LVOT obstruction, n (%)	11 (27.5)	5 (50)	0.172
LVEF (%)	77.6 ± 9.2	68.6 ± 15.9	0.023
E/e′	11.9 ± 5.9	20.2 ± 17.0	0.016
RVSP (mmHg)	31.0 ± 11.8	52.5 ± 23.3	0.011
RV-free wall thickness (mm)	10.2 ± 1.9	9.8 ± 3.6	0.662
TAPSE (cm)	2.8 ± 0.5	2.3 ± 0.5	0.007
RV FAC (%)	41.2 ± 12.8	32.1 ± 10.0	0.042
Strain measurements			
LV GLS (%)	–14.1 ± 3.2	–12.7 ± 3.1	0.779
LV thickest segmental strain (%)	–13.3 ± 7.8	–5.0 ± 3.0	<0.001
RV free wall strain (%)	–22.2 ± 9.5	–12.7 ± 6.7	0.013
RV septum strain (%)	–8.5 ± 4.5	–8.2 ± 6.1	0.838

BMI = body mass index; eGFR = estimated glomerular filtration rate; FAC = fractional area change; GLS = global longitudinal strain; LA = left atrium; LV = left ventricle; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; RV = right ventricle; RVSP = right ventricular systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

analysis, the LA volume index, LV mass index, LVEF, LV thickest segmental strain, TAPSE, RV FAC, and RV free wall strain were significantly associated with adverse composite events (model 1, Table 3). After adjusting for age and sex in the multivariable Cox regression analysis (model 2, Table 3), LVEF, LV thickest segmental strain, TAPSE, and RV free wall strain were independent predictors of adverse cardiovascular events. If we further adjusted for LVEF (model 3, Table 3), the prognostic significance remained in LV thickest segmental strain (HR, 95% CIs: 1.23, 1.01-1.51; p = 0.041), TAPSE (HR, 95% CIs: 0.24, 0.06-0.93; p = 0.039), and RV free wall strain (HR, 95% CIs: 1.17, 1.03-1.21; p = 0.006).

Among all the right-sided parameters, TAPSE yielded an area under the curve (AUC) of 0.76 (p = 0.005) and RV-free wall strain had an AUC of 0.78 (p < 0.001) in predicting long-term adverse composite events. Dichotomized by the optimal cutoff values derived from the ROC curve, RV free wall strain >–12.6% (HR 5.43; 95% CIs, 1.56-18.95; p = 0.008) had a significantly higher risk for developing composite events, whereas RV septal strain failed to have a prognostic value (HR 2.57; 95% CIs, 0.65-10.13; p = 0.178) (Fig. 2).

3.3. Predictive power and risk reclassification

Table 4 compares the predictive power for composite events between assessment of LV strain alone and the addition of RV functional evaluation. The addition of TAPSE or RV free wall LS improved AUC as the LV thickest segmental strain had an AUC of 0.81 (95% CIs: 0.67-0.91) in the prediction of adverse composite events. Assessment of RV systolic function resulted in an NRI of 31.4% (p = 0.035) by TAPSE and 34.1% (p = 0.010) by RV-free wall strain, compared with the assessment of LV alone (Table 4).

3.4. Reliability of RV strain measurements

Measurements of the RV global LS between the two independent observers exhibited good interobserver agreement (ICC: 0.81; 95% CIs, 0.59-0.92).

4. DISCUSSION

Our study showed that patients with composite events had significantly reduced LV thickest segmental strain and more impaired RV systolic function, as measured by TAPSE, FAC, and RV free wall strain. Both TAPSE and RV-free wall strain remained independent prognostic predictors of a higher risk of

Table 3

Univariate and multivariable analysis of echocardiography parameters predicting long-term composite events among patients with HCM on medical treatment

Variables	Model 1[a], HR (95% CI)	*p*	Model 2[b], HR (95% CI)	*p*	Model 3[c], HR (95% CI)	*p*
Left-sided chambers parameters						
LA volume index	1.04 (1.01-1.07)	0.019	1.03 (0.98-1.09)	0.201		
LV maximal wall thickness	1.05 (0.92-1.21)	0.457				
LV mass index	1.01 (1.002-1.02)	0.019	1.01 (1.00-1.02)	0.053		
LVEF	0.92 (0.87-0.98)	0.009	0.92 (0.86-0.98)	0.008	-	-
E/e′	1.04 (1.00-1.08)	0.053				
LV GLS	1.16 (0.92-1.49)	0.218				
LV thickest segment strain	1.24 (1.04-1.48)	0.016	1.25 (1.01-1.54)	0.037	1.23 (1.01-1.51)	0.041
Right-sided chambers parameters						
RVSP	1.05 (1.01-1.10)	0.024	1.04 (0.99-1.10)	0.099		
RV-free wall thickness	0.93 (0.85-1.20)	0.526				
TAPSE	0.19 (0.05-0.69)	0.012	0.27 (0.08-0.95)	0.041	0.24 (0.06-0.93)	0.039
RV FAC	0.94 (0.88-0.99)	0.039	0.95 (0.90-1.00)	0.053		
RV-free wall strain	1.13 (1.05-1.20)	0.001	1.13 (1.05-1.22)	0.001	1.17 (1.03-1.21)	0.006
RV septum strain	1.01 (0.89-1.15)	0.851				

CI = confidence interval; FAC = fractional area change; GLS = global longitudinal strain; HR = hazard ratio; LA = left atrium; LV = left ventricle; LVEF = left ventricular ejection fraction; RV = right ventricle; RVSP = right ventricular systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

[a]Model 1: crude ratios.

[b]Model 2: adjusted for age and sex.

[c]Model 3: adjusted for age, sex, and LVEF.

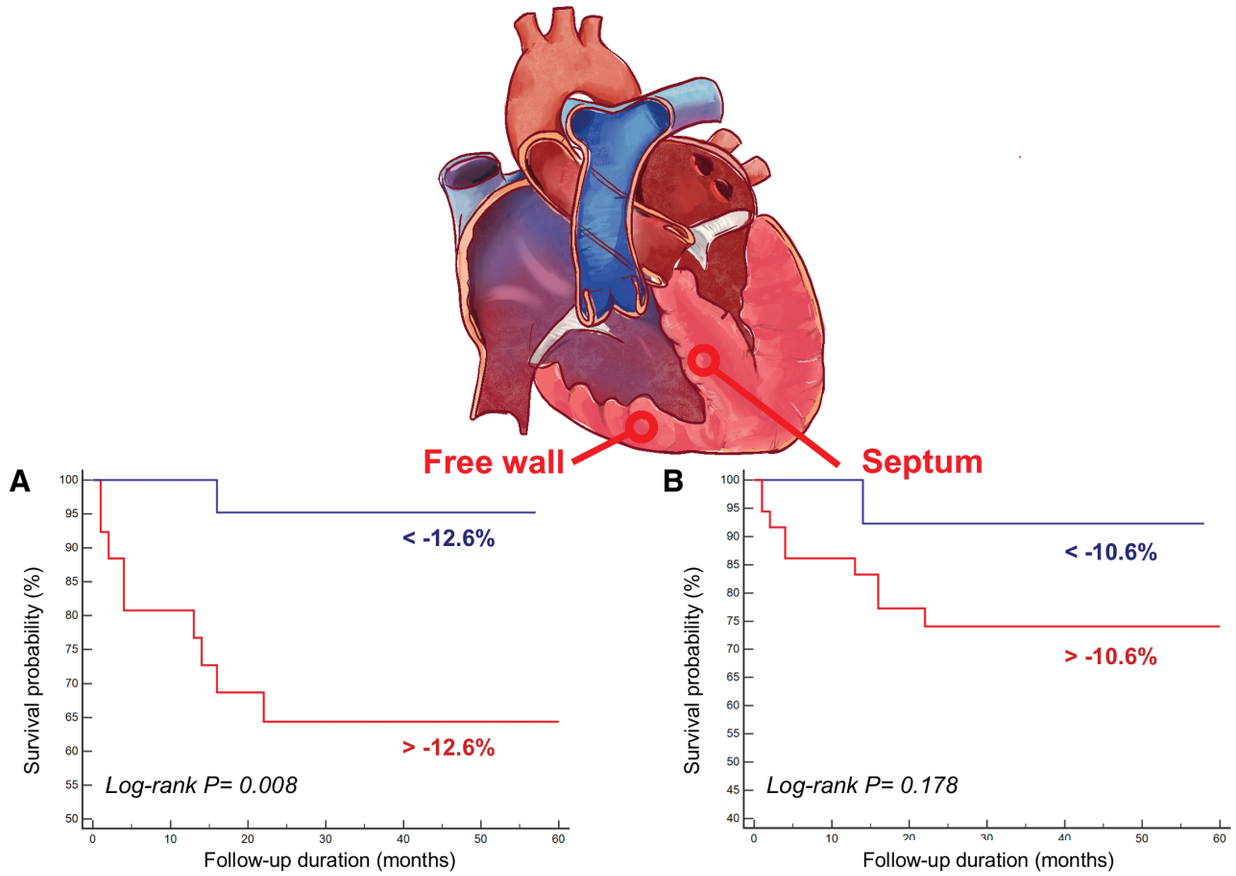

Fig. 2 Kaplan–Meier curves of the composite outcomes stratified by right ventricular segmental longitudinal strain. A, Free wall. B, Septum.

Table 4

Comparison of the predictive power of the composite events between assessing LV myocardial function alone and combined LV + RV myocardial function

Assessed parameters	AUC (95% CI)	NRI[a]	*p*
LV thickest segmental strain	0.811 (0.666-0.912)	(reference)	(reference)
+ TAPSE	0.820 (0.686-0.914)	0.314	0.035
+ RV-free wall strain	0.833 (0.700-0.923)	0.341	0.010

AUC = area under curve; CI = confidence interval; LV = left ventricle; NRI = net reclassification improvement; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion.
[a]The subjects were classified by the base risk prediction Cox model into low- and high-risk groups for the adverse cardiovascular events using the cutoff point of 0.33).

composite events, after adjusting for age, sex, and LVEF. The prognostic role of the RV-free wall was more evident than that of the RV septum. Our study demonstrated that the assessment of RV systolic function by echocardiography provided incremental prognostic significance over assessment of LV function alone, suggesting that comprehensive assessment of RV function could be useful for risk stratification in patients with HCM.

In the past decade, a multitude of studies has identified major clinical risk markers and stratified high-risk patients for SCD as candidates for implantable cardioverter-defibrillators. Contemporary management and preventive strategies have substantially reduced disease-related mortality rates.[22] Despite advancements in SCD prevention, there remains an entity of patients manifesting as symptomatic HF that requires frequent hospitalizations.[23] Although studies revealed that symptomatic HF is prevalent (approximately 50%-67%) among patients with HCM,[22] the predictors of HF hospitalization or other disease-related complications have not been comprehensively examined. Prior studies have identified echocardiographic indices as prognostic values. Ciabatti et al[23] demonstrated that larger LA volume at baseline was independently associated with more hospitalizations. A restrictive filling pattern and dilated LV end-diastolic diameter were also reported to be predictors of more cardiovascular deaths.[5,24] Compared with prior studies, our study showed that the eventful group had significantly larger LA volume and higher E/e′ ratio. In addition, our data revealed that the longitudinal strain of the thickest LV segment was more predictive of adverse events than the LV GLS in patients with HCM. Because myocardial disarray and fibrosis can only affect specific LV segments in HCM, our study suggested that segmental strain can be more reflective of the impact on regional myocardial deformation and can thus provide prognostic information among patients with HCM.[25] It should be noted that the prognostic role of LV GLS might not be manifested as in previous studies considering the limited case number in the present study.[26] As the superiority of LV regional longitudinal strain to LV GLS has been shown in patients with acute myocardial infarction,[27] The prognostic role of regional longitudinal strain in HCM warrants further exploration.

The incidence of RV involvement varied greatly by different methods and RV hypertrophy was found in around 44%-67% of patients with HCM through echocardiography.[9] Although RV involvement is prevalent in HCM, RV systolic function

measured by TAPSE or FAC is mostly within normal range or even surpassing the normal controls.[9] Since these conventional echocardiographic indices fail to demonstrate subtle RV dysfunction, early detection of RV systolic abnormalities by echocardiographic strain analysis becomes increasingly important in patients with HCM.[10] As Carlsson et al demonstrated that longitudinal displacement accounts for 80% of RV stroke volume, longitudinal shortening has been regarded as the main contributor to RV systolic function.[28] The reliability of RV longitudinal strain has been validated in a CMR study, the gold standard for assessing the complex crescent-shaped RV geometry.[29] RV longitudinal strain has been reported of prognostic significance in other cardiovascular diseases, including HF with reduced EF or after acute myocardial infarction.[11,30] The present study supported that RV longitudinal strain could be also a reliable predictor of adverse cardiovascular events among patients with HCM, and could provide incremental prognostic significance beyond assessing LV strain alone.

Furthermore, our study revealed that the prognostic value of RV longitudinal strain was mainly attributed to the change in RV-free wall myocardial deformation, whereas RV septal strain tracking from an RV approach failed to provide prognostic information.[19] Considering that RV septal strain can be dominated by the LV septum, the present study suggested that the compensatory longitudinal contraction of the RV-free wall could be a better parameter for risk stratification in patients with HCM. In addition, as TAPSE indicates RV basal free wall longitudinal function, this may explain why TAPSE had more prognostic significance than FAC, as shown in our study. However, it should be noted that a higher cutoff value of TAPSE, rather than 1.5 cm, should be adopted when assessing RV systolic function in patients with HCM.

The present study has several limitations. First, the registry enrolled a relatively small number of patients. Theoretically, studies that are adequately powered to a specific HCM-related outcome can be more practical for identifying at-risk patients who may benefit from a specific treatment. However, owing to the low event rate of any specific clinical endpoint in our patients with HCM, we adopted a composite of adverse events as the primary endpoint. Second, owing to the heterogeneity of genotypic composition and phenotypic expression observed in HCM, risk stratification based on currently identified risk factors may be incomplete. However, the unselected patients in the present study may be more representative of the overall spectrum of HCM. Third, the variability of echocardiographic strain analysis across vendor software platforms has become a major concern for its clinical applicability. Nevertheless, we used a vendor-independent software package for strain analysis in the present study to minimize diversity between vendors. Furthermore, limited by the tracking software used in the present study, data on RV segmental longitudinal strain were not available. Whether regional myocardial dysfunction of the RV has a further prognostic impact in patients with HCM requires further investigation. In addition, data from three-dimensional echocardiography or CMR were not sufficient for direct comparison with STE measurements. Future longitudinal follow-up studies can be considered to confirm the prognostic significance of RV systolic strain, as well as to illustrate whether impaired LA strain precedes RV strain deterioration.

In conclusion, impaired RV-free wall strain measured using STE could independently predict a higher risk of adverse cardiovascular events in patients with HCM. The present study suggests that comprehensive assessment of RV function adds incremental prognostic value to LV strain and is useful for risk stratification in addition to left-sided chamber parameters among patients with HCM.

ACKNOWLEDGMENTS

We thank the sonographers in the Taipei Veterans General Hospital Echocardiography Laboratory for their expertise and assistance. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A163.

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