Advanced echocardiographic techniques in hereditary cardiac diseases

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Chapter 5

Myocardial work in non-obstructive hypertrophic cardiomyopathy: implications for outcome

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Abstract

Aims. Non-invasive left ventricular (LV) pressure-strain loop (PSL) analysis is emerging as a new echocardiographic method to evaluate LV function, integrating longitudinal strain by speckle-tracking analysis and sphygmomanometrically-measured blood pressure to estimate myocardial work. Aims of this study were:1) to describe global and segmental myocardial work in HCM patients;2) to assess the correlation between myocardial work and other echocardiographic parameters;3) to evaluate the association of myocardial work with adverse outcomes.

Methods and results. 110 non-obstructive HCM patients (55±15 years,66% male), with different phenotypes (apical, concentric and septal hypertrophy), and 35 age- and sex-matched healthy controls were included. The following myocardial work indices were included: myocardial work index (MWI), constructive work (CW), wasted work (WW), cardiac efficiency (CE). The combined endpoint included all-cause mortality, heart transplantation, heart failure hospitalizations, aborted sudden cardiac death and appropriate implantable cardioverter defibrillator therapy. Mean global CW (1722±602 vs. 2274±574mmHg%, p<0.001), global CE (93(89-95) vs. 96(96-97)%, p<0.001) and global MWI (1534±551 vs. 1929±473mmHg%) were significantly reduced, while global WW (104(66-137) vs. 71(49-92)mmHg%,p<0.001) was increased in HCM patients compared to controls. Segmental impairment in CW co-localized with maximal wall thickness (HCM phenotype) and global CW correlated with LV wall thickness (r=-0.41,p<0.001), diastolic function (r=-0.27,p=0.001) and QRS duration (r=-0.28,p=0.001). Patients with global CW>1730 mmHg% (median value) experienced better event-free survival than those with global CW<1730 mmHg%(p<0.001).

Conclusion. Myocardial work, assessed non-invasively with echocardiography and blood pressure measurement, is reduced in non-obstructive HCM patients; it correlates with maximum LV wall thickness, and is significantly associated with worse long-term outcome.

Keywords: hypertrophic cardiomyopathy; myocardial work; left ventricular pressure strain loop; echocardiography

Introduction

Hypertrophic cardiomyopathy (HCM) is the most prevalent inherited cardiomyopathy and is characterized by increased myocardial wall thickness, accompanied by myocardial fiber disarray and interstitial fibrosis. These alterations lead to subtle myocardial systolic and diastolic dysfunction which are not always detectable by standard echocardiographic parameters.[1, 2] Previous studies have shown that left ventricular (LV) global longitudinal strain (GLS), measured by speckle-tracking echocardiography, is often impaired in HCM patients, despite a normal LV ejection fraction (LVEF), and is significantly correlated with the presence of myocardial fibrosis as assessed by cardiac magnetic resonance (CMR) imaging.[3] Moreover, impaired LV GLS has been associated with adverse outcomes in HCM patients, such as all-cause mortality, sudden cardiac death (SCD), heart failure and ventricular arrhythmias.[4-8] LV GLS however, remains a load-dependent measure of LV function, which might limit the assessment of LV performance under certain hemodynamic conditions, and when performing follow-up evaluations. A non-invasive technique of myocardial work estimation has been introduced as a novel method to evaluate myocardial performance. This approach takes into account both LV deformation and afterload by constructing a LV pressure-strain loop (PSL) which integrates non-invasively measured arterial blood pressure and longitudinal strain acquired by echocardiographic speckle-tracking analysis.[9-11] A first study showed that constructive work (CW) is impaired in patients with HCM and is associated with LV fibrosis as assessed by CMR.[12] However, segmental analysis of myocardial work has not been performed in these patients, despite the frequently heterogenous distribution of LV hypertrophy, and importantly, the potential prognostic value of these novel cardiac work measures is currently unknown. Therefore, the aims of this study were: 1) to describe global and segmental indices of myocardial work in HCM patients compared to healthy individuals; 2) to assess the correlation of myocardial work with other echocardiographic parameters; 3) to evaluate the association of myocardial work with adverse outcomes.

Methods

Study population

Patients with a diagnosis of HCM were identified from an ongoing clinical registry. HCM was diagnosed according to current guidelines: maximal LV hypertrophy (LVH) ≥15 mm (or ≥13 mm in case of affected first-degree relatives), which could not be explained by abnormal loading conditions.[1] Patients with obstructive HCM, defined as an LV outflow tract (LVOT) gradient ≥30 mmHg at rest or during provocation, were excluded. Patients were also excluded when speckle tracking was not feasible, or when non-invasive blood pressure values were not available at the time of the echocardiogram used for the calculation of myocardial work. Clinical data were collected from the departmental cardiology information system (EPD-Vision®; Leiden University Medical Center, Leiden, The Netherlands) and the first echocardiogram available was used for analysis. In addition, 35 healthy individuals with structurally normal hearts were selected from the echocardiography database as controls, and matched for age, sex and LVEF. The study complies with the Declaration of Helsinki. Due to the retrospective design of this study, the local ethics committee waived the need of individual, written informed consent.

Echocardiography

A commercially available ultrasound machine (Vivid E9, GE-Vingmed, Milwaukee, WI, USA) was used to perform standard 2-dimensional transthoracic echocardiography (TTE). Images were digitally stored and analyzed offline using proprietary software (EchoPac 202, General Electric Vingmed Ultrasound, Milwaukee, WI, USA). The LV dimensions, LV septal thickness, LV posterior wall thickness and left atrial (LA) diameter were measured from the parasternal long-axis view. Maximum LV wall thickness was assessed from short-axis views at different levels from base to apex to ascertain the different patterns of LVH. Septal HCM was diagnosed in the presence of asymmetric LVH, isolated to the septal and/or anteroseptal segments of the LV, while apical HCM was defined when LVH was limited to the apical segments of the LV. Concentric HCM was defined as symmetric LVH in all LV segments. LV volumes, LVEF and LA volume were measured using Simpson's method and indexed for body surface area (BSA).[13] LV diastolic function was assessed using Doppler mitral inflow peak E-wave velocity, divided by the peak early diastolic velocity (E') of the lateral mitral annulus, expressed as the E/E' ratio.[14] The grade of mitral regurgitation (MR) was assessed by using a multiparametric approach, according to current recommendations.[15] LVOT peak gradient at rest was quantified by continuous wave Doppler. Peak systolic pulmonary artery pressure was estimated by adding the peak velocity of the tricuspid regurgitation jet on continuous wave Doppler to the right

atrial pressure (estimated by the diameter and percentage inspiratory collapse of the inferior vena cava).[16]

Myocardial Work

LV myocardial work was calculated by integrating longitudinal strain and sphygmomanometrically-measured blood pressure, as previously described by Russell et al.[10] LV longitudinal strain was measured using speckle-tracking analysis on the standard 2-, 3- and 4-chamber apical views. The region of interest was automatically created and manually adjusted when necessary. LV GLS was then calculated by averaging the peak longitudinal strain in 17 segments from the 3 apical views. The peak systolic LV pressure was assumed to be equal to the peak arterial systolic pressure, based on the brachial cuff blood pressure measurements. A non-invasive LV pressure-strain curve was then constructed by proprietary software (EchoPac 202, General Electric Vingmed Ultrasound, Milwaukee, WI) and adjusted according to the duration of the ejection and isovolumetric phases which were defined by the opening and closure of the mitral and aortic valves.

During the LV ejection period - defined as the period between mitral valve closure and mitral valve opening - the total work within the area of the LV PSL represented the global myocardial work index (GMWI), myocardial work performed during segmental shortening represented constructive work (CW), whereas myocardial work performed during segmental elongation represented wasted work (WW). During isovolumetric relaxation, this definition was reversed such that myocardial work during shortening was considered as WW and myocardial work during lengthening was considered CW. CW and WW were calculated for each LV segment, according to the 17-segment model, and the global CW and WW were calculated as the averages of the segmental values. Cardiac efficiency (CE) was then expressed as CW / (CW+WW) x 100% per segment and the global CE as an average of all segmental values (Figure 1). To evaluate segmental differences, the mid and basal segments were combined, as well as the apical segments, resulting in 7 segments: septal, antero-septal, inferior, lateral, posterior, anterior and apical.

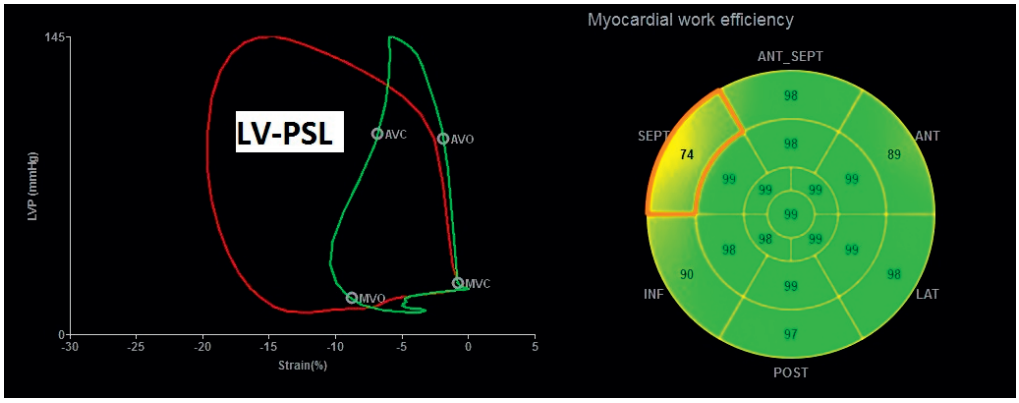

Figure 1. Examples of a left ventricular pressure strain loop (LV-PSL) and cardiac efficiency (CE). The red curve represents a normal LV-PSL, while the green curve reflects the deviating PSL of a septal segment in a HCM patient. The bulls-eye plot on the right, shows a significantly decreased CE in the septal segment.

Clinical outcomes

The endpoint of this study was a combined endpoint of all-cause mortality, heart transplantation, heart failure hospitalizations, aborted SCD and appropriate implantable cardioverter defibrillator (ICD) therapy. Aborted SCD was defined as a successful resuscitation from cardiac arrest with documented ventricular arrhythmias, while appropriate ICD therapy was defined as shock or anti-tachycardia pacing for ventricular arrhythmias. The occurrence of events during follow-up was obtained from survival status in municipal civil registries, review of medical charts and liaison with general practitioners.

Statistical analysis

Continuous variables are presented as mean ± standard deviation when normally distributed or as median (interquartile range) when not normally distributed. Categorical variables are presented as absolute numbers and percentages. Differences in clinical and echocardiographic characteristics between HCM patients and controls were compared using the Student t test, Mann-Whitney U test or χ^2 test, as appropriate. Receiver operating characteristic (ROC) curves were constructed to determine which myocardial work parameter had the highest area under the curve (AUC) to predict outcome. A Kaplan-Meier curve was then constructed to estimate the cumulative survival free of the endpoint and compared by log-rank test between patients with CW above the median (>1730 mmHg) and patients with CW below the median (<1730 mmHg). The correlation of CW with other clinical and echocardiographic parameters was assessed using Pearson's method or Spearman's method for continuous normally distributed, and ordinal and continuous non-normally distributed

parameters, respectively. Segmental differences between the various HCM phenotypes were analysed with the ANOVA and Kruskal Wallis tests. Intra-class correlation coefficients (ICC) were calculated for inter-observer and intra-observer agreement in 10 randomly selected patients, in order to evaluate reproducibility. Statistical analysis was performed with SPSS (version 23, IBM Corp, Armonk, NY, USA). P-values <0.05 were considered statistically significant.

Results

Study population

The study population consisted of 145 individuals: 110 patients diagnosed with HCM (55±15 years, 66% male) and 35 healthy controls (52±16 years, 51% male). Clinical characteristics of both groups are presented in Table 1. By definition, no differences were observed between the 2 groups regarding age and sex. Compared to controls, HCM patients showed slightly higher systolic blood pressure values and longer QRS duration. Previous atrial fibrillation was reported in 19 HCM patients (17%); 22 patients (20%) had heart failure symptoms (NYHA class II or more) and 21 patients (19%) had received an ICD.

Table 1. Clinical and ECG characteristics of HCM patients and controls.

	Controls N=35	**HCM patients N=110**	**p-value**
Clinical characteristics			
Age (years)	52±16	55±15	0.450
Men [n(%)]	18 (51)	73 (66)	0.159
Systolic BP (mmHg)	126±18	135±19	0.016
Diastolic BP(mmHg)	77±9	80±12	0.124
(Previous) Atrial fibrillation [n(%)]	0 (0)	19 (17)	0.007
NYHA class [n(%)]			0.002
I	35 (100)	88 (80)	
II	0 (0)	19 (17)	
III/IV	0 (0)	3 (3)	
ICD [n(%)]	0 (0)	21 (19)	0.002
ECG characteristics			
Heart rate (bpm)	66±11	66±11	0.964
QRS duration (ms)	94±10	109±25	0.001
LBBB/ RBBB [n(%)]	0 (0)	14 (13)	0.022
Ventricular pacing [n(%)]	0 (0)	11 (10)	0.066

BP blood pressure; ECG electrocardiography; HCM hypertrophic cardiomyopathy; ICD implantable cardioverter defibrillator; LBBB left bundle branch block; NYHA New York Heart Association; RBBB right bundle branch block

Standard echocardiographic characteristics

In Table 2 the echocardiographic characteristics are compared between HCM patients and healthy controls. HCM patients had a thicker interventricular septum and posterior wall, as well as a greater maximum LV wall thickness (19±5 mm vs 9±2 mm, p<0.001). Regarding different patterns of LVH, the majority expressed a septal phenotype (66%), followed by concentric HCM (24%), while apical HCM was observed in 10% of patients. LV dimensions were smaller in patients with HCM when compared to controls, while LA dimensions and volumes were higher in patients with HCM compared to controls. No differences were observed between HCM patients and controls regarding LVEF, although LV volumes were slightly lower in HCM patients and LV diastolic function was more often impaired. LV GLS was significantly impaired in HCM patients compared to controls (-14±5 vs -19±2%, p<0.001). Furthermore, MR grade ≥2 was observed in 17(16%) of the HCM patients and the LVOT gradient was within the normal range (as per inclusion criteria).

Table 2. Echocardiographic characteristics of HCM patients and controls.

	Controls N=35	**HCM patients N=110**	**p-value**
IVS (mm)	8 ± 2	18 ± 4	<0.001
PW (mm)	9 ± 1	12 ± 2	<0.001
Max LVH (mm)	9 ± 2	19 ± 5	<0.001
HCM phenotype [n(%)]			n/a
Septal	-	73 (66)	
Concentric	-	26 (24)	
Apical	-	11 (10)	
LVESV (ml)	45 ± 14	39 ± 15	0.032
LVEDV (ml)	116 ± 31	103 ± 29	0.039
LVEF (%)	61 ± 6	63 ± 10	0.331
LV GLS (%)	-19 ± 2	-14 ± 5	<0.001
LA diameter (mm)	34 ± 4	40 ± 6	<0.001
LAVI (ml/m²)	22 ± 6	36 ± 13	<0.001
E/E'	8 (6-9)	10 (7-14)	<0.001
Resting LVOT gradient (mmHg)	5 (3-5)	7 (5-11)	<0.001
MR ≥ grade 2 [n(%)]	0 (0)	17 (16)	0.013
sPAP (mmHg)	22 (18-26)	25 (21-31)	0.003

IVS interventricular septum; LA left atrial; LAVI left atrial volume index; LVEDV left ventricular end-diastolic volume; LVEF left ventricular ejection fraction; LVESV left ventricular end-systolic volume; LV GLS; left ventricular global longitudinal strain; LVOT left ventricular outflow tract; MR mitral regurgitation; PW posterior wall; sPAP systolic pulmonary artery pressure;

Myocardial work: global indices

Global myocardial work indices are summarized in Fig. 2. HCM patients showed significantly lower values of GMWI (1534±551 vs. 1929±473mmHg%, p<0.001) and global LV CW compared to controls (1722±602 mmHg% vs 2274±574 mmHg%, p<0.001) as well as higher values of global LV WW (104(66-137) mmHg% vs 71(49-92) mmHg%, p<0.001). This resulted in a lower global LV CE with a median of 93(89-95)% for HCM patients, compared to 96(96-97)% for controls (p<0.001).

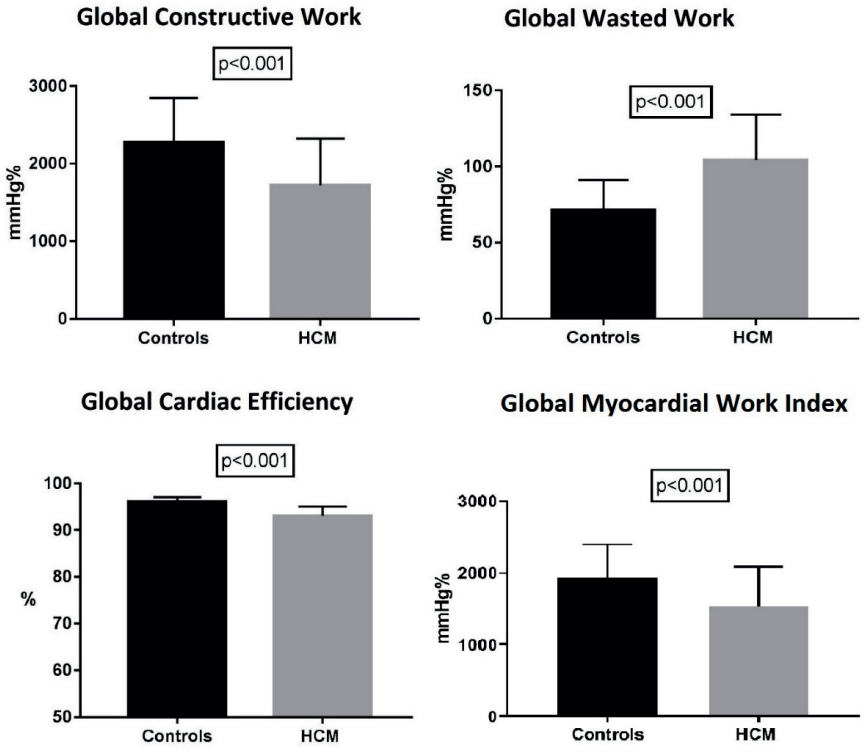

Figure 2. Myocardial work parameters in controls and hypertrophic cardiomyopathy (HCM) patients.

Correlation of global constructive work with other parameters

Global CW showed significant correlation with LA volume index (LAVI, r= -0.37, p<0.001), maximum LV wall thickness (r= -0.41, p<0.001), LV diastolic function (r= -0.27, p=0.001) and QRS duration (r= -0.28, p=0.001). Global CW showed also a high correlation with LV GLS (r=0.85, p<0.001). However, global CW was not significantly related with LV volumes (LVEDV, r= 0.034, p=0.681; LVESV, r= -0.11, p=0.187)

Association of global constructive work with outcomes

During a median follow-up of 5.4 (3.0-7.8) years, 24 patients (22%) reached the combined endpoint: 1 patient underwent a heart transplant, 1 patient experienced aborted SCD, 10 patients had appropriate ICD therapy, 1 patient was admitted for heart failure and 11 patients died. The cause of death was cardiac in 4 patients, non-cardiac in 3 patients and unknown in the remaining 4 patients. In order to assess which of the global myocardial work parameters had the strongest association with the endpoint, ROC curves were constructed. LV GLS showed an AUC of 0.74 (95% 0.63-0.85, p<0.001) and GMWI also showed a good association with the endpoint with an AUC of 0.77 (95% CI 0.66-0.87, p<0.001). However, global LV CW had the largest AUC of 0.78 (95% CI 0.68-0.88, p<0.001), while global LV WW showed no significant association with the endpoint with an AUC of 0.53 (95% CI 0.39-0.68, p=0.61) and global CE showed a borderline association with the endpoint with an AUC of 0.63 (95% CI 0.48-0.77, p=0.06). Subsequently, survival analysis was performed using global LV CW. When using the median value of the study population, patients with more impaired global LV CW (< 1730mmHg%) had a significantly worse survival free of the endpoint compared to patients with more preserved global LV CW (> 1730 mmHg%) (log-rank 11.2, p<0.001), as shown in Figure 3.

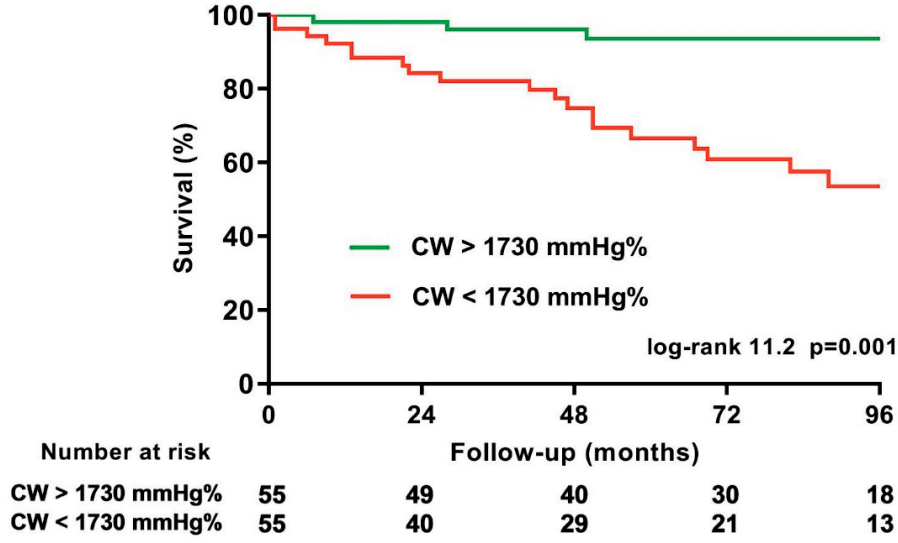

Figure 3 Kaplan-Meier survival curves depicting time to cumulative, event-free survival (all-cause mortality, aborted sudden cardiac death, heart failure hospitalizations and appropriate implantable cardioverter-defibrillator therapy) in patients with hypertrophic cardiomyopathy. Data are shown according to left ventricular constructive work (CW) >1730 mmHg% and CW <1730 mmHg% (median value).

Intra- and inter-observer variability of myocardial work parameters

The ICC for repeated measurements by the same observer (intra-observer agreement) was excellent for GLS (0.98(0.92-0.99), p<0.001), GMWI (0.97 (0.92-0.97), p<0.001) and global CW (0.99(0.96-0.99), p<0.001) and good for global WW (0.82 (0.27-0.96), p=0.009) and global CE (0.86(0.43-0.97), p=0.004); the ICC for measurements between two different observers (inter-observer agreement) was also excellent for GLS (0.97(0.88-0.99), p<0.001), GMWI (0.96 (0.89-0.97), p<0.001) and global CW (0.97(0.89-0.99),p<0.001) and good for global WW (0.76(0.05-0.94),p=0.022) and global CE (0.91(0.65-0.98), p=0.001)

Myocardial work: segmental analysis

Segmental values of myocardial work parameters are presented in Table 3 and compared between HCM patients and healthy controls. In LV all segments, CW was lower in patients with HCM as compared to controls. Interestingly, differences in WW were less evident. Only in the apical and anterior segments, WW was higher in HCM patients compared to controls, while in the other segments no differences in WW were observed between the two groups. The segmental CE was significantly lower for HCM patients in the apical, anteroseptal, posterior, lateral and anterior segments compared to controls. Regarding the septal segments, CE was not significantly different between HCM patients (94(90-98)%) and controls (95(93-97)%).

Table 3. Segmental analysis of myocardial work parameters in HCM compared to controls. * p-value < 0.05

	Constructive work (mmHg%)		Wasted Work (mmHg%)		Cardiac efficiency (%)	
	Controls	**HCM**	**Controls**	**HCM**	**Controls**	**HCM**
Apical	2670 ± 792	2068 ± 922*	43 (24-77)	102 (54-188)*	98(96-99)	94(90-97)*
Septal	1813 ± 472	1354 ± 606*	77 (50-103)	60 (22-119)	95(93-97)	94(90-98)
Anteroseptal	2107 ± 575	1521 ± 613*	56 (30-103)	73 (32-148)	97-94-98)	94(86-98)*
Inferior	2050 ± 500	1652 ± 669*	70 (35-133)	61 (21-139)	96(93-98)	96(90-98)
Posterior	2246 ± 729	1676 ± 758*	88 (40-207)	111 (49-223)	94(92-98)	93(85-96)*
Lateral	2160 ± 559	1625 ± 666*	55 (27-102)	80 (31-151)	97(95-98)	95(89-98)*
Anterior	2077 ± 684	1466 ± 733*	35 (21-72)	76 (29-134)*	98(96-98)	94(85-98)*

Figure 4 shows the segmental CW in the different HCM phenotypes. In patients with apical HCM, CW of the apical segments (1123±747 mmHg%) was significantly lower compared to patients with septal HCM (2255±860 mmHg%) and concentric HCM (1946±920 mmHg%), p<0.001. Similarly, septal CW was lower in patients with septal HCM (1385±579 mmHg%) and concentric HCM (1126±479

mmHg%) compared to patients with apical HCM (1693±860 mmHg%, p=0.025). In patients with concentric HCM, all segments (except for the apical segments) tended to have lower values of CW, although this difference was statistically significant only for the inferior segments (1408±584 mmHg% in concentric HCM vs. 1691±636 mmHg% in septal HCM and 1980±905 mmHg% in apical HCM, p=0.040).

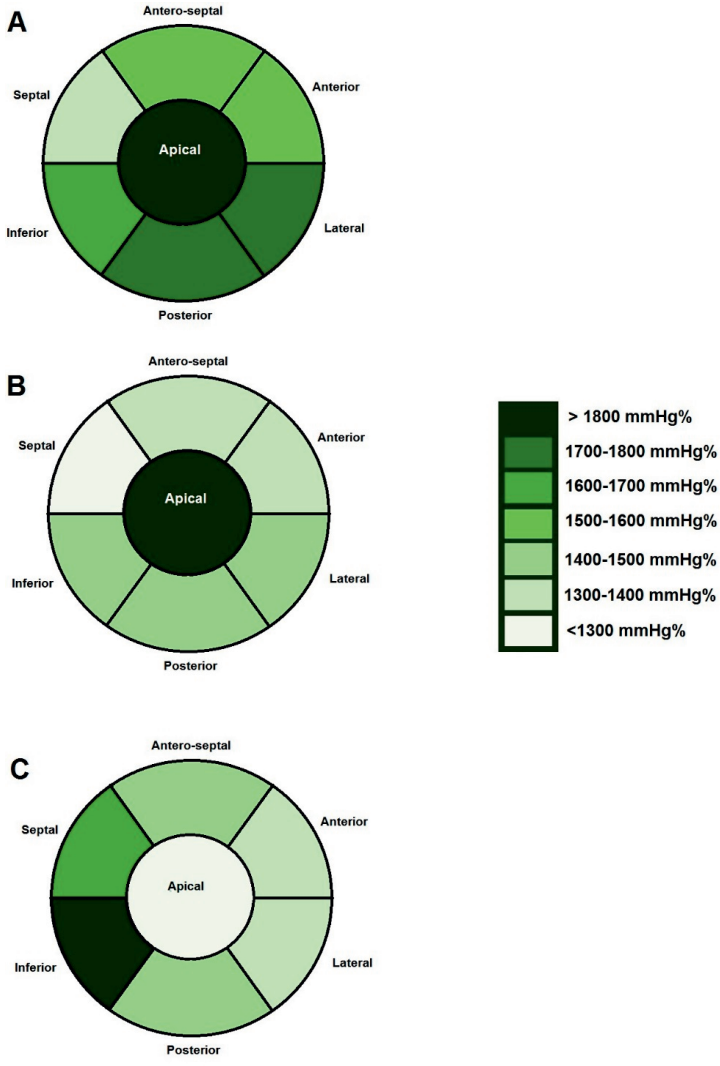

Figure 4. Segmental analysis of left ventricular constructive work for different hypertrophic cardiomyopathy (HCM) phenotypes.
Panel A septal HCM, ***Panel B*** concentric HCM, ***Panel C*** apical HCM

Discussion

The main findings of the present study can be summarized as follows: 1) HCM patients showed impaired values of global LV myocardial work parameters – GMWI, CW, WW and CE – when compared to healthy individuals, 2) global LV CW showed a correlation with maximum LV wall thickness, diastolic function and QRS duration and was significantly associated with adverse outcomes; 3) segmental differences of CW were observed in different HCM phenotypes.

Myocardial work in HCM

HCM is characterized by LV hypertrophy, myocardial fiber disarray and interstitial fibrosis, which can all significantly affect LV diastolic and systolic function, without an overt impairment of LVEF.[17] Consequently, several echocardiographic measurements have been proposed to better assess LV function in HCM patients. Over the past few years, LV GLS, as derived from speckle-tracking analysis, has emerged as a promising measure of LV function in patients with HCM and has shown a good correlation with histologically-proven myocardial fibrosis.[18] Moreover, several studies have demonstrated the prognostic value of LV GLS for predicting adverse outcomes in HCM patients.[3-8] However, LV GLS remains load-dependent, which might represent a limitation in case of changes in the hemodynamic conditions.[19] Myocardial work has been introduced as a new parameter of LV function, that takes into account the LV deformation as well as the LV afterload by constructing a LV-PSL based on non-invasive LV pressure (sphygmomanometric blood pressure) measurements. Russell et al.[10] validated this method against invasive LV pressure measurements and the LV-PSL area demonstrated a robust correlation with myocardial metabolism when assessed with positron emission tomography.

Several studies have already applied myocardial work measurements to various cardiac conditions.[12, 20-25] A study by Chan et al.[24] evaluated GMWI in patients with different loading conditions (i.e. with hypertension or ischemic and non-ischemic cardiomyopathies). In this study, patients with hypertension showed higher GWI compared to controls, whereas global CE was preserved due to a proportional increase in global CW and global WW. In a study by Van der Bijl et al,[23] the prognostic value of global CE in patients referred for cardiac resynchronization therapy (CRT) was evaluated. Lower values of global CE were associated with better outcome after CRT, likely reflecting the potential correction of LV dyssynchrony and recruitment of contractile reserve obtained with CRT in these patients. Only a single study evaluated myocardial work in HCM patients: Galli et al.[12] showed that global CW was reduced in 82 HCM patients as compared to controls (1599 ± 423 vs 2248 ± 249 mmHg%, p<0.001), while global WW was similar between HCM patients and controls (141±125 vs 101±88 mmHg%, p=0.18). The present study found similar values of global CW, which were

significantly reduced in HCM patients compared to controls. The values of global WW in HCM patients observed in the present study were also similar to the ones reported by Galli et al,[12] but we measured lower values of global WW in controls, accentuating the difference of global WW between HCM patients and. Galli et al.[12] demonstrated that a global CW of <1623 mmHg% was predictive of myocardial fibrosis on CMR, which might also explain the correlation of CW with diastolic dysfunction and LV thickness observed in the current study. In addition, a correlation between global CW and QRS duration was found probably reflecting the influence of (mild) LV dyssynchrony on myocardial work parameters. However, the association of myocardial work to clinical outcomes has never been evaluated in HCM patients, and the current results demonstrate a significant association of global CW with clinical outcomes.

Moreover, the present study evaluated segmental differences of myocardial work in HCM patients. CW was impaired in all myocardial segments when compared with healthy individuals. Interestingly, WW was only significantly impaired in the apical and anterior segments, whereas it was comparable to controls in the remaining segments. Since WW is mostly affected by dyssynchrony[9] and the prevalence of left or right bundle branch block was low in the current population (13%), relatively preserved values of WW were observed, in line with the findings of Galli et al.[12] Similarly, CE (defined as the ratio of CW divided by CW+WW), showed only mildly impaired values in most myocardial segments. Thus, CW was the most impaired myocardial work parameter in HCM patients, on both a global and segmental level. Moreover, differences of CW were also observed in different HCM phenotypes: patients with apical HCM had the most impaired CW in the apical segments, while in patients with septal and concentric HCM the CW was preserved the in apical segments, but impaired in the other segments. Segmental CW might therefore also be helpful to identify the specific HCM phenotype.

Clinical implications

The introduction of myocardial work parameters in the routine assessment of HCM patients might improve our understanding of cardiac performance in these patients, at both global and segmental levels, overcoming the load-dependency of other echocardiographic parameters by incorporating afterload. This is particularly relevant in patients with HCM, since afterload might change with medication use or geometrical changes and increase of wall thickness over time. This would provide clinicians a more sophisticated tool to refine follow-up of LV function in these patients, when blood pressure might vary between visits, and to assess the potential effect of different therapies. Furthermore, it might also represent a new risk-stratification tool to assess prognosis in HCM patients. Global CW might help especially in identifying 'low-risk' patients since a cumulative event-

free survival of 97% after 5 years was observed for patients with global CW >1730 mmHg%, whereas event-free survival was only 64% after 5 years in patients with global CW <1730 mmHg%.

Limitations

Several limitations of the current study should be mentioned. Some patients were excluded since blood pressure measurements were not available at the same the time of echocardiography; few patients were excluded when speckle-tracking analysis failed. Therefore we cannot exclude that this issue introduced a bias in the assessment. Furthermore, patients with obstructive HCM were excluded, since the estimated LV PSL based on the non-invasive measured blood pressure, does not reflect accurately LV pressure in these patients.[10] Further prospective research is required to confirm our results and establish the clinical utility of myocardial work parameters in HCM.

Conclusion

Myocardial work, assessed non-invasively with echocardiography and blood pressure measurement, is impaired in HCM. Global LV CW is correlated with maximum LV wall thickness, diastolic function and QRS duration and is significantly associated with adverse outcomes. Characteristic segmental patterns of CW can be depicted in different HCM phenotypes.

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