Myocardial Work Combined with a Cardiopulmonary Exercise Test is a Useful Prognostic Assessment of Patients with Non-obstructive Hypertrophic Cardiomyopathy

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Research Article

Keywords: Myocardial work, Cardiopulmonary exercise test, Hypertrophic cardiomyopathy, Prognostic assessment

Posted Date: July 13th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3126500/v1

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Abstract

Background

The aim of this study was to evaluate the prognosis of patients with non-obstructive hypertrophic cardiomyopathy (HCM) using myocardial work combined with a cardiopulmonary exercise test (CPET). The association between myocardial work and CPET parameters and left ventricular wall thickness was investigated. To achieve the study aim, 55 patients with non-obstructive HCM and 55 healthy control participants were enrolled. Echocardiographic data were collected and compared, and a CPET was performed separately for patients with HCM and controls. Differences in CPET and myocardial work parameters and changes in myocardial work parameters from before to after the CPET were compared between the two groups.

Results

Global longitudinal strain, global work index, global constructive work (GCW), and global work efficiency parameters were significantly reduced and longitudinal strain peak time dispersion (PSD) was prolonged in patients with HCM compared to controls ($P < 0.001$). No difference in global wasted work was observed between the two groups ($P > 0.05$). Regarding CPET parameters, peak oxygen uptake, anaerobic threshold, oxygen pulse, and metabolic equivalents were significantly lower in the HCM group compared with the control group ($P < 0.05$). The slope of carbon dioxide ventilation equivalent was higher in patients with HCM, but the between-group difference was not significant ($P > 0.05$). After the CPET, there was a significant increase in PSD, but not GCW, in the HCM group, while there was a significant increase in GCW, but not PSD, in the control group. Maximal wall thickness showed a significant positive correlation with PSD ($r = 0.84$, $P < 0.001$), a significant negative correlation with GCW ($r = -0.84$, $P < 0.001$), and a weak negative correlation with peak oxygen uptake ($r = -0.45$, $P < 0.001$).

Conclusion

Myocardial work combined with a CPET can provide a valid assessment of the prognosis of patients with HCM. The effective myocardial work and CPET parameters are negatively correlated with left ventricular wall thickness.

Background

Hypertrophic cardiomyopathy (HCM) is the most common hereditary cardiomyopathy, characterized by hypertrophy of cardiomyocytes, increased thickness of the ventricular wall, and associated myocardial fiber disorders and interstitial fibrosis, resulting in impaired left ventricular (LV) deformation [1]. Many patients with non-obstructive HCM and preserved ejection fraction did not have significant symptoms at rest in the early period; some patients present to the hospital for examination due to limitations in daily
exercise or activity. HCM is the most common cause of sudden death in young people, including trained athletes [2], and is considered an important cause of sudden arrhythmic death, heart failure, atrial fibrillation, and cerebral infarction [3]. Early, effective, and rapid evaluation of cardiac function in patients with HCM is imperative for its treatment. In contrast, conventional echocardiography often fails to detect abnormal changes in LV systolic function in patients with HCM at the early stage. Therefore, more sensitive and comprehensive techniques are needed to detect cardiac function in patients with HCM.

Previous studies have shown that LV global longitudinal strain (GLS) measured using speckle tracking echocardiography is frequently impaired in patients with HCM [4, 5], and significantly correlated with myocardial fibrosis assessed using cardiac magnetic resonance imaging [6]. However, LV GLS is a load-dependent measure of LV function, and myocardial work is derived from the LV pressure-strain loop (PSL). PSL combines non-invasive measurements of arterial blood pressure and overall longitudinal strain, taking into account both LV deformation and afterload [7]. The cardiopulmonary exercise test (CPET) is a recognized safe clinical management tool [8] with good utility for risk stratification and prognostic assessment of patients with suspected or confirmed HCM [9–11]. The aims of this study were to evaluate the prognosis of patients with HCM using myocardial work performed in combination with the CPET and investigate the correlation between myocardial work and CPET parameters and LV wall thickness.

Results

Comparison of clinical characteristics

Clinical characteristics of both groups are presented in Table 1. There was no significant difference in age, sex, body mass index (BMI), body surface area (BSA), blood pressure, or heart rate between the two groups (P > 0.05). Nine patients (16.4%) with HCM showed symptoms of heart failure [New York Heart Association (NYHA) functional class II]. Atrial fibrillation was reported in six patients with HCM (10.9%).

Table 1 Clinical characteristics of patients with HCM and control participants
### Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control participants (n=55)</th>
<th>Patients with HCM (n=55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>44.7±9.8</td>
<td>46.9±10.9</td>
<td>0.170</td>
</tr>
<tr>
<td>Sex, male</td>
<td>38 (69.1)</td>
<td>40 (72.7)</td>
<td>0.675</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.9±2.4</td>
<td>25.7±2.5</td>
<td>0.118</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.7±0.1</td>
<td>1.8±0.1</td>
<td>0.496</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>127±14.3</td>
<td>131.6±15.2</td>
<td>0.120</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>78.6±10.6</td>
<td>81.5±11.0</td>
<td>0.160</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>I</td>
<td>55 (100)</td>
<td>46 (83.6)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>0 (0)</td>
<td>9 (16.4)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

### ECG characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control participants (n=55)</th>
<th>Patients with HCM (n=55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>73.7±8.1</td>
<td>77.0±10.0</td>
<td>0.060</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0 (0)</td>
<td>6 (10.9)</td>
<td>0.027</td>
</tr>
</tbody>
</table>

HCM: hypertrophic cardiomyopathy; BMI: body mass index; BSA: body surface area; SBP: systolic blood pressure; DBP: diastolic blood pressure; NYHA: New York Heart Association; ECG: echocardiogram.

Data are expressed as mean±standard deviation or number(percentage).

**Comparison of conventional echocardiographic parameters**

As shown in Table 2, there was no significant difference in LV end diastolic diameter (LVEDd), LV end systolic diameter (LVESd), or LV ejection fraction (LVEF) between the two groups (P > 0.05), whereas left atrial diameter (LAD) and left atrial volume index (LAVI) were higher in patients with HCM compared with control participants. Patients with HCM had greater maximum LV wall thickness (P < 0.001), and LV diastolic function was more often impaired in patients with HCM. The septal and lateral wall side annular peak velocity during early diastole (e') were reduced in the HCM group compared to the control group, and peak velocity during early diastole (E)/e' were significantly increased in the HCM group (P < 0.001).
Table 2 Echocardiographic parameters of patients with HCM and control participants

<table>
<thead>
<tr>
<th>Echocardiographic parameters</th>
<th>Control participants (n=55)</th>
<th>Patients with HCM (n=55)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD, mm</td>
<td>30.4±3.0</td>
<td>41.0±4.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAVI, mL/m²</td>
<td>26.4±2.6</td>
<td>37.9±4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MWT, mm</td>
<td>9.6±0.9</td>
<td>19.3±3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDd, mm</td>
<td>46.3±6.7</td>
<td>42.6±4.9</td>
<td>0.392</td>
</tr>
<tr>
<td>LVESd, mm</td>
<td>28.2±5.3</td>
<td>26.6±3.6</td>
<td>0.403</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>63.6±5.6</td>
<td>65.5±8.3</td>
<td>0.162</td>
</tr>
<tr>
<td>E, cm/s</td>
<td>71.2±20.9</td>
<td>67.3±21.3</td>
<td>0.013</td>
</tr>
<tr>
<td>A, cm/s</td>
<td>66.7±12.3</td>
<td>77.1±19.4</td>
<td>0.168</td>
</tr>
<tr>
<td>Septal e', cm/s</td>
<td>7.6±1.6</td>
<td>4.9±1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lateral e', cm/s</td>
<td>9.9±2.6</td>
<td>6.3±1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/e'</td>
<td>9.1±2.7</td>
<td>12.8±5.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAD: left atrial diameter; LAVI: left atrial volume index; MWT: maximum wall thickness; LVEDd: left ventricular end diastolic diameter; LVESd: left ventricular end systolic diameter; LVEF: left ventricular ejection fraction; E: peak velocity during early diastole; A: peak velocity during late diastole; e’: annular peak velocity during early diastole.

Data are expressed as mean±standard deviation.

Comparison of strain and myocardial work parameters

GLS (-14.1±2.2%), GWI (1466.1±424.4 mmHg%), GCW (1386.2±470.9 mmHg%), and GWE (86.3±4.8 %) were significantly lower and PSD (68.6±21.4 ms) was significantly higher in the HCM group than in the control group (P < 0.001). GWW increased in the HCM group, but the between-group difference was not statistically significant (P > 0.05), as shown in Table 3.
**Table 3** Strain and myocardial work characteristics of patients with HCM and control participants

<table>
<thead>
<tr>
<th>Strain and MW parameters</th>
<th>Control participants (n=55)</th>
<th>Patients with HCM (n=55)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS %</td>
<td>-18.0±1.9</td>
<td>-14.1±2.2</td>
<td>0.001</td>
</tr>
<tr>
<td>PSD, ms</td>
<td>46.10±12.8</td>
<td>68.6±21.4</td>
<td>0.001</td>
</tr>
<tr>
<td>GWI, mmHg%</td>
<td>1949.1±248.3</td>
<td>1466.1±424.4</td>
<td>0.001</td>
</tr>
<tr>
<td>GCW, mmHg%</td>
<td>2258.8±348.3</td>
<td>1386.2±470.9</td>
<td>0.001</td>
</tr>
<tr>
<td>GWW, mmHg%</td>
<td>199.2±94.7</td>
<td>226.1±100.5</td>
<td>0.220</td>
</tr>
<tr>
<td>GWE, %</td>
<td>94.9±2.2</td>
<td>86.3±4.8</td>
<td>0.001</td>
</tr>
</tbody>
</table>

MW: myocardial work; GLS: global longitudinal strain; PSD: longitudinal strain peak time dispersion; GWI: global work index; GWE: global work efficiency; GCW: global constructive work; GWW: global wasted work.

Data are expressed as mean±standard deviation.

**Comparison of cardiopulmonary exercise testing parameters**

Among the 55 patients with HCM, 45 were terminated due to lower extremity fatigue, 3 due to ST segment changes, 4 due to systolic blood pressure (SBP) ≥220 mmHg, and 3 (patients with atrial fibrillation) due to an abnormal blood pressure response. In the control group, 54 participants were terminated due to lower extremity fatigue and 1 due to ST segment changes.

Peak oxygen uptake (VO$_2$), anaerobic threshold (AT), oxygen pulse (VO$_2$/HR), and metabolic equivalent of tasks (METs) were significantly lower in the HCM group compared with the control group (all $P<0.001$), and the carbon dioxide ventilation equivalent (VE/VCO$_2$) slope was slightly higher compared with the control group, but the difference was not statistically significant ($P>0.05$), as shown in Table 4.
Table 4 CPET parameters of patients with HCM and control participants

<table>
<thead>
<tr>
<th>CPET parameters</th>
<th>Control participants (n=55)</th>
<th>Patients with HCM (n=55)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO$_2$, (mL/min/kg)</td>
<td>25.8±4.2</td>
<td>18.6±5.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AT, (mL/min/kg)</td>
<td>16.5±2.7</td>
<td>12.4±2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VE/VCO$_2$ slope</td>
<td>27.8±4.9</td>
<td>29.8±5.2</td>
<td>0.102</td>
</tr>
<tr>
<td>VO$_2$/HR, mL/beat</td>
<td>11.9±1.8</td>
<td>9.7±2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>METs</td>
<td>6.8±1.2</td>
<td>4.7±1.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CPET: cardiopulmonary exercise test; Peak VO$_2$: peak oxygen uptake; AT: anaerobic threshold; VE/VCO$_2$ slope: slope of carbon dioxide ventilation equivalent; VO$_2$/HR: oxygen pulse; METs: metabolic equivalents.

Data are expressed as mean±standard deviation.

Comparison of myocardial work parameters and PSD before and after the cardiopulmonary exercise test

Myocardial work parameters and PSD before and after the CPET are summarized in Figure 3. There was no statistically significant difference in GCW (1386.2±470.9 vs 1399.7±424.2 mmHg%, P=0.875) and GWW (226.1±100.5 vs 260.6±100.7 mmHg%, P=0.075) before the CPET compared to after in the HCM group, while PSD significantly increased (68.6±21.4 vs 92.4±14.0 ms, P<0.001). In the control group, GCW significantly increased after the CPET relative to before (2258.8±348.3 vs 2628.3±381.6 mmHg%, P<0.001), whereas the changes from pre- to post-exercise in GWW (199.2±94.8 vs 217.2±109.6 mmHg%, P=0.359) and PSD ( 46.1±12.8 vs 50.1±10.3 ms, P=0.074) were not statistically significant.

Correlations of MWT with PSD, GCW, and peak VO$_2$

MWT showed a significant positive correlation with PSD (r =0.84, P<0.001), a significant negative correlation with GCW (r =-0.84, P<0.001), and a weak negative correlation with peak VO$_2$ (r =-0.45, P<0.001) (Figure 4).

Intra- and inter-observer variability of strain and myocardial work parameters

Ten cases each from the control and HCM groups were randomly selected. The intraclass correlation coefficients for repeated measurements showed good repeatability for GLS, PSD, GWI, GCW, GWW, and GWE between the intra- and inter-observer (Table 5).
### Table 5 Intra- and inter-observer variability of strain and myocardial work parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Intra-observer</th>
<th>Inter-observer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICC  95%CI</td>
<td>ICC  95%CI</td>
</tr>
<tr>
<td>GLS</td>
<td>0.936 0.845 0.974</td>
<td>0.921 0.811 0.968</td>
</tr>
<tr>
<td>PSD</td>
<td>0.840 0.640 0.934</td>
<td>0.817 0.594 0.923</td>
</tr>
<tr>
<td>GWI, mmHg%</td>
<td>0.945 0.867 0.978</td>
<td>0.954 0.887 0.981</td>
</tr>
<tr>
<td>GCW, mmHg%</td>
<td>0.955 0.890 0.982</td>
<td>0.930 0.831 0.971</td>
</tr>
<tr>
<td>GWW, mmHg%</td>
<td>0.834 0.628 0.931</td>
<td>0.816 0.593 0.923</td>
</tr>
<tr>
<td>GWE, %</td>
<td>0.904 0.775 0.961</td>
<td>0.884 0.732 0.953</td>
</tr>
</tbody>
</table>

GLS: global longitudinal strain; PSD: peak strain time dispersion; GWI: global work index; GWE: global work efficiency; GCW: global constructive work; GWW: global wasted work; ICC: interclass correlation coefficient; CI: confidence interval.

### Discussion

Patients with HCM have a highly heterogeneous clinical presentation, with dyspnea, chest pain, palpitations, and syncope being the more common symptoms, and sudden death events occurring in severe cases. Regardless of symptoms, the American Heart Association guidelines recommend that patients with HCM optimize their lifestyle by performing light-to-moderate intensity aerobic exercise to help improve cardiorespiratory health and quality of life [12]. Therefore, the assessment of LV function and exercise tolerance is particularly important. The main findings of this study may be summarized as follows: (1) Strain and myocardial work parameters are impaired in patients with HCM compared to the healthy population, and myocardial work can be used to assess LV function; (2) CPET parameters are impaired in patients with HCM compared to healthy populations, and the CPET enables the safe assessment of exercise tolerance; and (3) MWT is associated with PSD, GCW, and Peak VO$_2$, and the combination of myocardial work and the CPET allows for better prognostic assessment of patients with HCM.

Pathogenic variants in the genes encoding the protein components of myofascicular segments are the main cause of HCM, resulting in myocardial hypertrophy in different parts of the LV wall due to differences in gene expression and regional wall stress [13].

Cardiomyocyte hypertrophy and disorganized myocardial fiber arrangement reduce wave conduction velocity and cause asynchronous LV myocardial contraction. The present study showed a significant decrease in GLS and increase in PSD in the HCM group, indicating delayed myocardial electrical activity and reduced mechanical activity in patients with HCM and significantly impaired LV deformation, consistent with the findings of Hiemstra et al [14]. Concurrently, the damage to myocardial synchrony is aggravated by reduced oxygen supply due to coronary microvascular dysfunction within the
hypertrophied myocardium and medial hypertrophy of small intramural arteries. Further, the abnormal electromechanical motion limits the mechanical efficiency of LV ejection, increases energy loss, and reduces the effective work done by the myocardium. The present study showed that the LV myocardial work parameters – GWI, GCW, and GWE – were significantly lower in the HCM group than in the control group, which is consistent with the results of previous studies [15]. GWW was slightly increased in patients with HCM compared to controls, but this difference did not reach statistical significance, likely because LV systolic function was still in the compensatory phase, which is consistent with the findings of Galli et al. [16]. Galli et al. also showed that GCW in patients with HCM was associated with the localization and overall amount of myocardial fibrosis assessed using cardiac magnetic resonance gadolinium delayed enhancement scanning. Further, these authors suggested that alterations in GCW may reflect myocardial fiber disorders and impaired myocardial metabolism in patients with HCM, making GCW a major predictor of LV fibrosis [16].

The CPET is a non-invasive simultaneous test of the cardiovascular and respiratory systems during exercise to assess the exercise capacity of patients. Most studies examining the prognostic value of the CPET have used Peak VO$_2$ as the primary measure of cardiopulmonary endurance [17, 18]. Compared to the subjective limitations of the NYHA classification, Weber and Janicki proposed a more objective classification for cardiac function during exercise based on peak VO$_2$ and AT [19]. In this study, the cardiorespiratory exercise test parameters – peak VO$_2$, AT, VO$_2$/HR, and METs – were found to be significantly lower in the HCM group compared to the control group. The decrease in peak VO$_2$ in patients with HCM is attributed to increased heart rate, myocardial oxygen consumption, and oxygen demand, and reduced left atrial strain during exercise [20], which prevents an effective increase in the volume per beat and causes an imbalance in oxygen supply and demand. Concurrently, myocardial hypertrophy causes limited coronary flow reserve [21], which further aggravates myocardial hypoxia and causes a decrease in peak VO$_2$. In the present study, there was an increase in VE/VCO$_2$ slope in the HCM group; however, the change was not statistically significant, probably because most of the patients in the HCM group were NYHA functional class I, in the early stage of the disease, and did not show symptoms of heart failure. Elevated VE/VCO$_2$ slope is common in patients with heart failure, and the mechanism of its occurrence may be related to decreased cardiac output and increased ventilatory dead space and mismatched pulmonary ventilation and perfusion due to microvascular insufficiency of the pulmonary vascular bed [22].

In this study, we found a significant increase in PSD, but not GCW, in patients with HCM with an increase in blood pressure during the CPET. Peak VO$_2$ is the main correlate of GCW [16]. This study found that patients with HCM who performed regular daily exercise had a high peak VO$_2$ that almost met the oxygen demand of the exercising myocardium. Further, the myocardium was able to contract effectively with high GCW, and the exercise tolerance was similar to that of the control group. In contrast, those with low peak VO$_2$ have significantly lower exercise tolerance because the myocardial oxygen demand is not effectively met by exercise, and myocardial ineffective contraction increases.
In addition, this study found that peak VO$_2$, METs, and GCW were significantly lower, and GLS and PSD were significantly higher in those with an abnormal blood pressure response during the CPET, associated with exercise-induced LV systolic dysfunction, a rapid reduction in cardiac output, and consequently, hemodynamic instability, associated with a high risk of sudden cardiac death.

Several limitations of the present study should be mentioned. First, this study is a single-center study with a small sample size, and further exploration in multi-center studies with large sample sizes are required in future. Second, the patients with HCM were not studied separately according to hypertrophic phenotype. In addition, no follow-up assessment of patients with HCM was performed.

**Conclusion**

In summary, patients with HCM can adapt their lifestyle to the pathology-related exercise limitations based on their own myocardial work parameters and CPET results to reduce the incidence of sudden cardiac death events. Myocardial work combined with the CPET can effectively evaluate the prognosis of patients with HCM.

**Methods**

**Study Population**

Fifty-five patients with non-obstructive HCM [40 males, 15 females, aged 22–66 (44.7 ± 9.8) years], diagnosed at the Longyan First Affiliated Hospital of Fujian Medical University from January 2022 to March 2023 were selected. HCM was diagnosed according to the 2014 ESC Guidelines [5]: wall thickness ≥ 15 mm in LV myocardial segments (or ≥ 13 mm in cases of affected first-degree relatives) that could not be explained by abnormal loading conditions. The exclusion criteria were as follows: NYHA functional class ≥ IV, resting blood pressure ≥ 180/100 mmHg (poor control of medications), combined with acute myocardial infarction, any condition that does not tolerate exercise, patients who have undergone surgical LV outflow tract evacuation or septal alcohol ablation, obstruction of the left or middle LV outflow tract, hypertension, aortic stenosis, or other distinct diseases causing cardiac hypertrophy.

A control group was also selected comprising 55 healthy volunteers [38 males, 17 females, aged 25–63 (46.9 ± 10.9) years] with normal 12-lead electrocardiogram (ECG) and echocardiogram and matched for age and sex. All participants signed a written informed consent form, and the study was approved by the hospital ethics review committee (approval number: LYREC2022-015-03).

**Conventional echocardiography and myocardial work**

GE Vivid E95 color Doppler ultrasound diagnostic apparatus (GE Medical Systems, Milwaukee, WI, United States) with an M5Sc-D probe (frequency 1.5–4.5 MHz) was used. Images were digitally stored and analyzed offline using EchoPAC 203 workstation. Participants were placed in the left lateral recumbent position and connected to the limb lead ECG. When the patient's respiration and heart rate were stable,
the patient's age, height, and weight were entered, and the BSA was calculated. The LVEDd, LVESd, LAD, MWT at end-diastole, LVEF measured using Simpson's method, mitral valve early diastolic flow E peak (E), mitral valve late diastolic flow A peak (A), mitral annulus early diastolic septal side, and lateral wall-side peak velocity (e') were measured from the parasternal long-axis view and four-chamber apical views. Then, the mean E/e' was calculated. All parameter measurements and analyses were conducted in accordance with the American Society of Echocardiography and the British Society of Echocardiography guidelines [23, 24].

The probe was placed on the apical part of the heart, and apical four-chamber, three-chamber, and two-chamber heart images were acquired and stored for three consecutive cardiac cycles.

The images were imported into EchoPac 203 image analysis software, and the endocardium of the apical four-chamber, two-chamber, and three-chamber heart images were traced, the width of the region of interest was adjusted to wrap around the entire myocardium, and the systolic and diastolic pressures of the patient's brachial artery were entered. The software automatically measured and calculated the overall LV GLS (Fig. 1), PSD, GWI, GCW, GWW, GWE, and PSL (Fig. 2).

Cardiopulmonary exercise test

Participants' height and weight were recorded, and BMI was calculated. A symptom-limited bicycle exercise test with standard incremental power was performed using a cardiopulmonary exercise system (Nanjing HigherMed Health Technology Co., Ltd., China) under the supervision of a cardiologist. The process included 3 min rest, 3 min no load, and 60 r/min speed cycling warm-up, followed by cycling at a constant speed to maintain 15–30 W/min incremental load power until the maximum exercise endurance (6–10 min) was achieved, then the recovery period was entered to maintain a cycling speed of 30–40 r/min for > 5 min. The gas collation mask was worn during exercise and connected to the volume sensor. The exhaled breath was continuously and automatically collected and analyzed through a gas sampling tube to continuously monitor heart rate, blood pressure, oxygen saturation, and 12-lead ECG. Peak VO$_2$, AT, VO$_2$/HR, and METs are indicators of exercise tolerance and were derived at the end of the exercise test. The VE/VCO$_2$ slope was also derived and is an indicator of gas exchange. An abnormal blood pressure response to exercise was defined as an increase in peak SBP of < 20 mmHg from baseline and a decrease in SBP from baseline during recovery from exercise [25].

The exercise test was terminated under the following conditions: (1) The patient presented with chest pain, dyspnea, dizziness, palpitations, pain in the lower extremities, or fatigue and asked for termination; (2) ECG showed horizontal or downward sloping depression of the ST segment in adjacent leads ≥ 0.2 mV for ≥ 2 min; (3) Decrease in SBP ≥ 10 mmHg, SBP consistently below baseline with increasing power, SBP ≥ 220 mmHg, and/or diastolic blood pressure ≥ 110 mmHg; and (4) Severe arrhythmias, such as ventricular tachycardia, multiple premature ventricular beats, second or third degree atrioventricular conduction block, or sinus arrest.
Statistical Analysis

Statistical analysis was performed using SPSS version 26 (IBM, Armonk, NY). Continuous variables are expressed as means ± standard deviations. Comparisons between groups were made using two independent samples Student’s t-tests. Continuous variables with skewed distribution were denoted by M (\(P_{25}, P_{75}\)), and the Mann–Whitney U test was used for comparison between two groups. Categorical variables are expressed as frequencies and percentages, and comparisons between groups were made using \(\chi^2\) or Fisher’s exact test. Correlation analyses were performed using Pearson’s correlation coefficient. Intraclass correlation coefficients were calculated for inter-observer and intra-observer agreement in 20 randomly selected patients to evaluate reproducibility. \(P\) values < 0.05 were considered to indicate statistical significance.

Abbreviations

HCM  Hypertrophic cardiomyopathy

CPET  Cardiopulmonary exercise test

GLS  Global longitudinal strain

PSD  Longitudinal strain peak time dispersion

GWI  Global work index

GCW  Global constructive work

GWE  Global work efficiency

GWW  Global wasted work

Peak VO\(_2\)  Peak oxygen uptake

AT  Anaerobic threshold

VO\(_2\)/HR  Oxygen pulse

METs  Metabolic equivalents

VE/VCO\(_2\) slope  Slope of carbon dioxide ventilation equivalent

MWT  Maximal wall thickness

PSL  Pressure-strain loop

ECG  Electrocardiograph
BMI  Body mass index
BSA  Body surface area
SBP  Systolic blood pressure
DBP  Diastolic blood pressure
NYHA  New York Heart Association
LAD  Left atrial diameter
LAVI  Left atrial volume index
LV  Left ventricular
LVEDd  Left ventricular end diastolic diameter
LVESd  Left ventricular end systolic diameter
LVEF  Left ventricular ejection fraction
E  Peak velocity during early diastole
A  Peak velocity during late diastole
e'  Annular peak velocity during early diastole

Declarations

Ethics approval and consent to participate
The study was approved by the Research Ethics Committee of Longyan First Affiliated Hospital of Fujian Medical University (approval number: LYREC2022-015-03).

Consent for publication
Not applicable.

Availability of data and materials
The datasets supporting the conclusions of this article are included within the article.

Competing interests
The authors declare that they have no competing interests.
Funding

This study was supported by Starup Fund for scientific research, Fujian Medical University (Grant number: 2021QH1340).

Author contributions

Performed the literature review: YFL, SHH; conducted the echocardiography measurements: SHH, YFL; conducted the cardiopulmonary exercise test: BW; selected participants and collected the clinical data: LYF, SHH, JTL, JHC; performed data analysis: SHH, YFL; wrote the manuscript: YFL, SHH; reviewed the manuscript: ZTT, SHQ, DPC, JLH. All authors have read and approved the final manuscript.

Acknowledgements

The authors thank Alice for the English language editing.

References


Figures
Figure 1

Two-dimensional images of apical four-chamber heart and GLS bull's eye plot of patients with HCM and control participants. A and D: apical hypertrophy, B and E: asymmetric hypertrophy, C and F: control participants. GLS: global longitudinal strain; HCM: hypertrophic cardiomyopathy.
Figure 2

LV PSL and GWI bull's eye plot of patients with HCM and control participants. A: apical hypertrophy, B: asymmetric hypertrophy, C: control participants. The area under the PSL curve decreased in HCM patients, indicating that GWI was impaired. LV: left ventricular; PSL: pressure-strain loop; GWI: global longitudinal strain; HCM: hypertrophic cardiomyopathy.
Figure 3
Myocardial work parameters and PSD before and after the cardiopulmonary exercise test in patients with HCM and control participants. PSD: longitudinal strain peak time dispersion; HCM: hypertrophic cardiomyopathy.

Figure 4
Scatter plot of correlations between MWT and PSD, GCW, and Peak VO\textsubscript{2}. MWT: maximal wall thickness; PSD: longitudinal strain peak time dispersion; GCW: global constructive work; Peak VO\textsubscript{2}: peak oxygen uptake.