Significance of Maximal and Regional Left Ventricular Wall Thickness in Association With Arrhythmic Events in Patients With Hypertrophic Cardiomyopathy

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**Background:** Increased maximal left ventricular wall thickness (LVWT; >30 mm) is a marker of risk for sudden cardiac death in hypertrophic cardiomyopathy (HCM). Patients with mild left ventricular hypertrophy (LVH) are not free of events. Regional heterogeneity of LVH may contribute to arrhythmic vulnerability.

**Methods and Results:** 157 HCM patients underwent assessment of maximal and regional LVWT by 2-dimensional echocardiography, and arrhythmic burden in a follow-up of a median 3.7 years. 45 patients with ventricular arrhythmic events (VAEs+ group) had larger maximal LVWT and regional LVWTs (basal anterior-B12 and equatorial inferior-EQ6 segments, P=0.05). Maximal LVWT and B12 above a cut-off value of 15mm were associated with a significant 4.5-fold (95% confidence interval (CI) 1.1–18.8, P=0.04), 3.2-fold (95%CI 1.5–6.7, P<0.002), and EQ6 above 19mm with 5.9-fold (95%CI 2.0–16.9, P<0.001) increased the relative risk of VAEs. Multivariate analysis identified the 2 regional measures as the only predictors, independently associated with arrhythmic risk.

**Conclusions:** Non-invasive imaging measures, such as LVWT, do have a role in identifying the patients at risk of VAEs. In addition to maximal LVWT, the key regional LVWTs provide complementary information of incremental value to the conventional risk stratification model. (Circ J 2010; 74: 531–537)

**Key Words:** Hypertrophic cardiomyopathy; Left ventricular wall thickness; Ventricular tachyarrhythmias
34.7±12.8
39.8±13.7
9
NS
NS
NS
3
<0.05*
NS
<0.05*
NS
7
<0.05*
NS
NS
9
P value
NS
NS
P value
NS
NS
26
NS
<0.0001*
VAEs+ (n=45)
51x53
Milwaukee, WI, USA). All arrhythmias, including those of
48-h ambulatory ECG monitoring (Marquette Electronics,
a routine 2-channel (CM1 on channel 1 and V
At study entry and annually thereafter, all patients underwent
Holter Monitoring
performed by 2 independent observers, unaware of the
diastole.
greatest thickness in the LV in any single segment at end-
and apical level (AP)). Maximal LVWT was defined as the
 maximal and regional LVWTs in parasternal short-axis views
for global systolic function, we obtained the
tional indices of global systolic function, we obtained the
of Echocardiography guidelines.
Doppler measurements in accordance with American Society
views were used to obtain M-mode, 2-dimensional, and
imaging variables were considered by univariate and multi-
categorical data are expressed as proportions. Com-
Continuous data are expressed as mean ± standard deviation
Statistical Analysis
Continuous data are expressed as mean ± standard deviation
(SD); categorical data are expressed as proportions. Com-
parisons of the means between patients with and without
arrhythmic events were made using the unpaired Student’s
t-test or 1-way ANOVA for continuous variables; categorical
variables were tested with Chi-square and Fisher exact tests.
All tests were 2-tailed; probability values of P<0.05 were
considered significant. Predictive associations of clinical and
ingage variables were considered by univariate and multi-
variate stepwise (forward likelihood) logistic regression
analysis. SPSS statistical software (SPSS Inc, Chicago, IL,
USA, version 15.0) was used for the statistical analysis.

Results
Clinical Characteristics, Events and Treatment
During the follow-up 45 VAEs were documented (9 aborted
and 7 completed VF arrests; 29 NSVTs, out of which 3 were
polymorphic VT) (Table 1). Patients with VAEs comprised
the VAEs positive group (VAEs+); those without events
served as controls (VAEs− group). Patients in the 2 groups
were well matched for age, sex and presenting symptoms
(Table 2). Despite taking more sotalol and amiodarone,
patients with events suffered from palpitations to a signifi-
cantly greater extent (Table 2). Table 3 includes.

exclusion of significant epicardial coronary artery disease by
invasive coronary angiography was dictated by the clinical
judgement in the relevant majority of subjects (n=123) by the
presence arrhythmia, anginal or syncopal symptoms,
traditional risk factors (age, smoking, high cholesterol),
decrease in blood pressure (BP) on risk-assessment exercise
testing (n=40), or peri-procedurally for myectomy/transcor-
ary ablation of septal hypertrophy (TASH).

Transthoracic Echocardiography
All patients were imaged in the left lateral decubitus position
using an Acuson 128 XP/10 (Mountain View, CA, USA)
or GE Vingmed system V (GE Ultrasound Europe). Standard
views were used to obtain M-mode, 2-dimensional, and
Doppler measurements in accordance with American Society
of Echocardiography guidelines. In addition to conventional
indicators of global systolic function, we obtained the
maximal and regional LVWTs in parasternal short-axis views
from 10 LV segments (at 3 o’clock–lateral wall, 6 o’clock–
inferior wall, 9 o’clock–septal wall, and 12 o’clock position–
Anterior wall) at 3 different levels (basal B, equatorial (EQ)
and apical level (AP)). Maximal LVWT was defined as the
greatest thickness in the LV in any single segment at end-
diastole. Echocardiographic studies and measurements were
performed by 2 independent observers, unaware of the
arrhythmic outcomes.

Holter Monitoring
At study entry and annually thereafter, all patients underwent
a routine 2-channel (CM1 on channel 1 and V on channel 2
48-h ambulatory ECG monitoring (Marquette Electronics,
Milwaukee, WI, USA). All arrhythmias, including those of
supraventricular and ventricular origin, were recorded. Ven-
tricular tachycardias (VT) were classified as sustained or non-
sustained. Non-sustained ventricular tachycardia (NSVT) was
defined as 3 or more consecutive ventricular beats at a rate
≥120 beats/min, lasting <30s. Patients continued their medi-
cation while on Holter monitoring, including β-blockers and
antiarrhythmic therapy. In addition to annual 48-h Holter
recordings, any otherwise documented events on ECG (VT,
ventricular fibrillation (VF) and SCD) in prospective fol-
low-up of a median 3.7 years (range 0–143 months) were
included.

Statistical Analysis
Continuous data are expressed as mean±standard deviation
(SD); categorical data are expressed as proportions. Com-
parisons of the means between patients with and without
arrhythmic events were made using the unpaired Student’s
t-test or 1-way ANOVA for continuous variables; categorical
variables were tested with Chi-square and Fisher exact tests.
All tests were 2-tailed; probability values of P<0.05 were
considered significant. Predictive associations of clinical and
imaging variables were considered by univariate and multi-
variate stepwise (forward likelihood) logistic regression
analysis. SPSS statistical software (SPSS Inc, Chicago, IL,
USA, version 15.0) was used for the statistical analysis.

Table 1. Patients’ Characteristics

<table>
<thead>
<tr>
<th></th>
<th>VAEs− (112)</th>
<th>VAEs+ (45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>68 (60.7%)</td>
<td>25 (55.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>34.7±12.8</td>
<td>39.8±13.7</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea (NYHA &gt;II)</td>
<td>38 (31.7%)</td>
<td>16 (43.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Family Hx of SCD/HCM</td>
<td>77 (64.2%)</td>
<td>22 (59.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Chest pain</td>
<td>39 (32.5%)</td>
<td>15 (39.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Palpitations</td>
<td>27 (22.5%)</td>
<td>14 (37.8%)</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Syncope</td>
<td>27 (23.7%)</td>
<td>11 (27.9%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* t-test, P<0.05 is considered significant.

NYHA, New York Heart Association; Hx of SCD/HCM, history of
SCD/hypertrophic cardiomyopathy. Other abbreviations see in
Table 1.

Table 3. Treatments in the Study Population

<table>
<thead>
<tr>
<th>Medications</th>
<th>VAEs− (112)</th>
<th>VAEs+ (45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>59 (52.7%)</td>
<td>11 (49.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>14 (12.3%)</td>
<td>7 (16.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>β-blockers</td>
<td>14 (12.3%)</td>
<td>6 (14.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Sotalol</td>
<td>2 (1.8%)</td>
<td>3 (7%)</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>17 (14.9%)</td>
<td>14 (32.6%)</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Disopyramydol</td>
<td>4 (3.5%)</td>
<td>2 (4.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myectomy</td>
<td>3 (2.6%)</td>
<td>4 (8.9%)</td>
<td>NS</td>
</tr>
<tr>
<td>TASH</td>
<td>1 (0.9%)</td>
<td>5 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Permanent pacemaker*</td>
<td>2 (1.8%)</td>
<td>1 (2.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>ICD (25 in total)</td>
<td>8 (7.1%)</td>
<td>17 (37.8%)</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

* t-test, P<0.05 is considered significant.

TASH, transcoronary ablation of septal hypertrophy; ICD, implant-
able cardioverter device. Other abbreviation see in Table 1.
### Table 4. Measures of Conventional Echocardiography

<table>
<thead>
<tr>
<th>Measurements</th>
<th>VAEs– (112)</th>
<th>VAEs+ (45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVED</td>
<td>44.1±5.8 (111)</td>
<td>43±6.9 (45)</td>
<td>NS</td>
</tr>
<tr>
<td>LVES</td>
<td>25.7±6.7 (111)</td>
<td>23.8±6.9 (45)</td>
<td>NS</td>
</tr>
<tr>
<td>FS</td>
<td>43±9.4 (111)</td>
<td>45.12±10.3 (45)</td>
<td>NS</td>
</tr>
<tr>
<td>LA size</td>
<td>40.2±7.6 (111)</td>
<td>42.9±7.5 (45)</td>
<td>0.05*</td>
</tr>
<tr>
<td>LVOT gradient (resting)</td>
<td>100 (87%)</td>
<td>35 (84%)</td>
<td>NS</td>
</tr>
<tr>
<td>SAM (resting)</td>
<td>39 (34.2%)</td>
<td>17 (39.5%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Pattern**

<table>
<thead>
<tr>
<th>VAEs– (111)</th>
<th>VAEs+ (45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASH</td>
<td>54 (48.2%)</td>
<td>26 (58%)</td>
</tr>
<tr>
<td>Concentric</td>
<td>11 (9.8%)</td>
<td>7 (15.6%)</td>
</tr>
<tr>
<td>Apical</td>
<td>6 (5.4%)</td>
<td>2 (4.4%)</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>1 (0.9%)</td>
<td>2 (4.4%)</td>
</tr>
</tbody>
</table>

*P<0.05 is considered significant.

VAEs, ventricular arrhythmic events; LVED, left ventricular end-diastolic dimension; LVES, left ventricular end-systolic dimension; FS, fractional shortening; LA, left atrium; LVOT, left ventricular outflow tract; SAM, systolic anterior motion; ASH, asymmetric septal hypertrophy.

### Table 5. Maximal and Regional LVWT

<table>
<thead>
<tr>
<th>Analyzable segments</th>
<th>VAEs– (112)</th>
<th>VAEs+ (45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max LVWT</td>
<td>18±6.2 (112)</td>
<td>21.3±6.3 (45)</td>
<td>&lt;0.003*</td>
</tr>
<tr>
<td>B12</td>
<td>14.3±5.1 (107)</td>
<td>17.3±5.5 (44)</td>
<td>&lt;0.02*</td>
</tr>
<tr>
<td>B9</td>
<td>14.6±4.3 (80)</td>
<td>16.3±4.0 (34)</td>
<td>NS</td>
</tr>
<tr>
<td>B6</td>
<td>11.9±6.4 (108)</td>
<td>11.5±3.3 (44)</td>
<td>NS</td>
</tr>
<tr>
<td>B3</td>
<td>12.9±3.4 (65)</td>
<td>14.8±3.9 (27)</td>
<td>0.03*</td>
</tr>
<tr>
<td>EQ12</td>
<td>17.5±5.2 (108)</td>
<td>19.8±5.9 (42)</td>
<td>NS</td>
</tr>
<tr>
<td>EQ9</td>
<td>18.7±8.2 (79)</td>
<td>18.4±4.1 (33)</td>
<td>NS</td>
</tr>
<tr>
<td>EQ6</td>
<td>11.3±2.9 (107)</td>
<td>12.7±3.2 (42)</td>
<td>0.001*</td>
</tr>
<tr>
<td>EQ3</td>
<td>15.9±6.5 (67)</td>
<td>15.4±3.2 (26)</td>
<td>NS</td>
</tr>
<tr>
<td>AP12</td>
<td>18.1±6.7 (83)</td>
<td>18.0±5.4 (35)</td>
<td>NS</td>
</tr>
<tr>
<td>AP6</td>
<td>14.9±5.7 (81)</td>
<td>15.1±4.5 (34)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*P<0.05 is considered significant.

LVWT, left ventricular wall thickness, LVWT number, o’clock position in parasternal short-axis view; VAEs, ventricular arrhythmic events; B, basal slice; EQ, equatorial slice; AP, apical slice.

### Table 6. Univariate Predictors of All Events in HCM Patients: Clinical Variables and Measures of Non-Invasive Testing

<table>
<thead>
<tr>
<th>HR</th>
<th>Wald</th>
<th>Sig.</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.0</td>
<td>1.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>1.9</td>
<td>2.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Family Hx of SCD or HCM</td>
<td>0.9</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Chest pain</td>
<td>0.1</td>
<td>3.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Dyspnea (NYHA class &gt;I)</td>
<td>1.1</td>
<td>2.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Syncope</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Palpitations</td>
<td>1.2</td>
<td>3.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Max LVWT</td>
<td>1.0</td>
<td>1.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Max LVWT (cut-off: 15 mm)</td>
<td>4.5</td>
<td>4.3</td>
<td>0.041†</td>
</tr>
<tr>
<td>Max LVWT (cut-off: 19 mm)</td>
<td>1.2</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>LA size</td>
<td>1.0</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>LVED</td>
<td>1.0</td>
<td>0.1</td>
<td>0.8</td>
</tr>
<tr>
<td>LVES</td>
<td>1.2</td>
<td>0.1</td>
<td>0.8</td>
</tr>
<tr>
<td>FS</td>
<td>1.1</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>LVH pattern</td>
<td>1.2</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>SAM</td>
<td>1.1</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Mid cavity gradient</td>
<td>0.1</td>
<td>5.6</td>
<td>0.021†</td>
</tr>
<tr>
<td>LVOT Vmax</td>
<td>2.0</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>B LVWT12</td>
<td>1.1</td>
<td>5.8</td>
<td>0.021†</td>
</tr>
<tr>
<td>B LVWT12 (cut-off: 15 mm)</td>
<td>3.2</td>
<td>9.4</td>
<td>0.0021†</td>
</tr>
<tr>
<td>B LVWT 9</td>
<td>1.0</td>
<td>0.03</td>
<td>0.9</td>
</tr>
<tr>
<td>B LVWT 6</td>
<td>1.0</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>B LVWT 3</td>
<td>1.1</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>EQ LVWT 12</td>
<td>1.0</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>EQ LVWT 9</td>
<td>1.0</td>
<td>0.03</td>
<td>0.9</td>
</tr>
<tr>
<td>EQ LVWT 6</td>
<td>1.2</td>
<td>4.9</td>
<td>0.031†</td>
</tr>
<tr>
<td>EQ LVWT 6 (cut-off: 15 mm)</td>
<td>1.7</td>
<td>2.8</td>
<td>0.09</td>
</tr>
<tr>
<td>EQ LVWT 6 group (cut-off: 19 mm)</td>
<td>5.9</td>
<td>10.7</td>
<td>0.001†</td>
</tr>
<tr>
<td>EQ LVWT 3</td>
<td>1.0</td>
<td>0.1</td>
<td>0.8</td>
</tr>
<tr>
<td>AP LVWT 12</td>
<td>1.0</td>
<td>1.8</td>
<td>0.2</td>
</tr>
<tr>
<td>AP LVWT 6</td>
<td>1.2</td>
<td>2.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Logistic regression analysis: †P<0.05 is considered significant.

Non-invasive testing comprised 24-h Holter monitoring, and echocardiography.

HR, hazard ratio; CI, confidence interval; Vmax, maximal flow velocity by Doppler. Other abbreviations see in Tables 2, 4, 5.
Echocardiography
There were no significant differences among the conventional echocardiographic measures, including intracavity dimensions, global systolic function, the presence of flow-obstructive phenomena or the pattern of LVH distribution. The LA was significantly larger in the VAEs+ group (Table 4). Both groups showed hyperdynamic radial systolic function, expressed as fractional shortening, and a similar distribution of diastolic impairment.

Maximal and Regional Wall Thickness
Maximal LVWT was significantly greater in the VAEs+ group. Regionally, there was a significantly larger LVWT in the basal anterior (B12), basal lateral (B3) and inferior equatorial (EQ6) segments (Table 5).

Analysis of Relationships
The univariate predictors are listed in Table 6, Figure. Among the clinical variables, male sex, palpitations and dyspnea were associated with significantly greater risk of arrhythmic events. Maximal LVWT on its own provided no value in differentiating between those at risk or not. Yet, introducing a cut-off value of 15 mm rendered maximal LVWT15 mm with a 4.5-fold increase in the risk of VAEs (95% confidence interval (CI) 1.1–18.8, P=0.04). Regionally, B12 and EQ6 provided modest, but significant associations (B12: hazard ratio (HR) 1.1, 95%CI 1.0–1.2, P=0.02, EQ6: HR 1.2, 95%CI 1.0–1.2, P=0.03), further strengthened by cut-offs of 15 mm and 19 mm, respectively (B1215 mm: HR 3.2, 95%CI 1.5–6.7, P=0.002, EQ619 mm: HR 5.9, 95%CI 2.0–16.9, P=0.001). The presence of a mid-cavity gradient was associated with arrhythmic events; however, this was not linked with the absolute magnitude of the flow acceleration.

With the multivariate stepwise procedure, maximal LVWT15 mm provided a trend towards incremental value (HR 3, Wald 3.2, 95%CI 0.9–9.8, P=0.07), only when combined with traditional risk factors (male sex, family history of heart disease and BP response to exercise). Regional measures yielded significant models for both, B1215 mm and EQ619 mm (B1215 mm: HR 3.1, 95%CI 1.5–6.8, P=0.004; EQ619 mm HR 6.3,
LV Wall Thickness and HCM

95%CI 2.1–18.8, P=0.001), identifying these 2 regional measures as the only predictors, independently associated with arrhythmic events. Age, sex, family history of HCM/SCD, LA size, other regional LVWT, accelerated flow in the LVOT and BP response provided no significant contribution to the model. The presence of VEAs was the only independent predictor of ICD-implantation decision making (HR=0.4, 95%CI 0.2–0.5, P=0.0001).

Discussion

The present study aimed to assess the significance of maximal and regional LVWT in patients with HCM and directly compare the predictive value of these indices and contrast them with the conventional risk factors within the same patient group. The principal findings of our study are: (1) LVWT is an important determinant of risk; (2) in predicting VAEs risk, maximal LVWT complements traditional risk markers in a comprehensive risk stratification manner; and (3) regional LVWTs of key LV segments play an independent role in predicting arrhythmic events and provide incremental value in the risk stratification of VAEs in HCM patients.

The role of non-invasive imaging in identification of high-risk HCM patients remains an evolving field of crucial clinical utility. Measures used to describe LVH, a phenotypical hallmark of HCM, such as maximal LVWT, appear to be associated with arrhythmic vulnerability, and yet, the interpretation of findings of several longitudinal studies is at odds. Although markedly increased LVWT (≥30 mm) agreeably links with a high risk of SCD, head-to-head comparison with traditional risk factors in follow-on studies failed to reproduce its presumptive predictive power.1-3 The results of the present study shed some light on these uncertainties by demonstrating that maximal LVWT may be able to assist in reliable risk prediction, but only as part of an overall risk stratification model. In the patient group with arrhythmic events, overall maximal LVWT is remarkably greater, and those patients with maximal LVWT >15 mm have a significant 4.5-fold increased risk of VAEs. Yet, maximal LVWT appears to be a relatively non-specific measure, providing a meaningful contribution only in conjunction with traditional risk factors.

An important goal of non-invasive testing is not only identification of HCM patients at high risk, but also distinguishing those with a low arrhythmic event rate.11-13 A wide range in the 95%CI for maximal LVWT≤15 mm endows this index with poorly characterized prognostic power for excluding those at lower risk and, in line with previous reports, providing no benefit of exclusion of those with only mild LVH. Here, the regional distribution may offer more relevant information; B12>15 mm is associated with a respectably narrow range of 95%CI (and also EQ>6 mm, yet still short of statistical significance), indicating that regional measures represent a key addition of the present study. Strong association of these key segments with arrhythmia vulnerability markedly outperforms not only the maximal LVWT, but also the traditional risk factors, identifying these 2 measures of potentially more refined value in risk stratification strategies. No other segments provided similar associations. Whether these features are inherent to the 2 segments described needs revalidation through future studies.

The mechanisms of SCD in HCM are complex, in part because of the great variability in the extent of the arrhythmogenic substrate. Previous investigation into the electrophysiological characteristics of increased LVWT in the septal region have indicated the presence of a marked reduction in the bipolar voltage amplitude in the LV regions with extensive hypertrophy, as well as local conduction delay and conduction blocks.14 This is consistent with the notion that re-entrant ventricular arrhythmias, which lead to SCD, arise from a substrate that includes slowly conducting pathways that delay ventricular activation. The structural disruption and myofibrillar disarray seen in HCM would provide the conditions for unidirectional block and delay, setting the stage for lethal arrhythmia.15 To complicate matters further, various types of VAEs are associated with marked heterogeneity in the risk for SCD; whether NSVT, the predominant type of VAE in our study, represents a marker of malignant arrhythmia has also been hotly debated in many studies, which are best characterized by their heterogeneous design, populations with variety of presentations16-19 or their highly selected patients.20 To weigh the arrhythmic burden, others have attempted to capture the markers of risk for VAEs in terms of age,21 histopathological/electrophysiological substrates,22-24 or imaging yield,25 with the summative yield that VAEs have a low positive and a relatively high negative predictive value for SCD in HCM populations.25 Despite the overall low likelihood of a fatal event when VAEs are present, it is the detrimental, unexpected and sudden nature that warrants the ongoing search for superior and preferably non-invasive ways of identification of those at high risk of SCD. In line with this, our study adds value to characterization of the arrhythmic propensity associated with increased LVWT, demonstrating a close link with increased LVWT in key segments, over and above the conventional measures of risk.

Recent advances provide important new insights into the underlying pathophysiology of HCM, the regional heterogeneity of LV thickness, and the well-described hemodynamic pathophysiological macro- and microphenomena, such as intracavity flow obstruction, microvascular dysfunction, metabolic disturbances, and regional fibrosis.33-35 Little is known about the relationships of these with arrhythmic vulnerability. In particular, dynamic LVOT obstruction and its association with prognosis and SCD has been the subject of much research interest.7-9 It is estimated that 25% of patients with HCM have dynamic LVOT obstruction and when severe this can cause significant clinical symptoms, including dyspnea, chest pain and syncope,36 and can predispose to the development of atrial arrhythmias.6 Amongst others, Elliot et al looked into the relationship between the presence of LVOT obstruction and the risk of SCD/ICD and found that prognosis is worse when it is present.41 Adverse outcomes were related to the severity of obstruction and also associated with the presence of other recognized risk factors for SCD, perhaps indicating towards an indirect role for LVOT obstruction. This observation was further corroborated by the finding of the low SCD mortality in asymptomatic patients with LVOT obstruction and no other SCD risk markers. Moreover, although interventions to reduce LVOT obstruction provide some relief of symptoms when present, there is little evidence of improved prognosis in the absence of symptoms and other risk factors.42 The findings from the present cohort are in line with these previous studies, indicating similar distribution of procedures and devices in the both groups, with no association with VAEs.

Clinical Implications

Maximal LVWT may be an important predictor of arrhythmic risk; the results of our study shed some light on the caveat
of using a single and relatively non-specific parameter, such as maximal LVWT, in an estimation of arrhythmic risk. The role of maximal LVWT in risk stratification is appropriate in a multiparametric/multifactorial manner, providing incremental value only when combined with other conventional measures of risk, such as family history of SCD/HCM or adverse BP response to exercise. Another key contribution of this study is the finding that not every max LVWT value is important; its regional distribution may play a more relevant role in arrhythmic vulnerability. In this study, the regional measures of B125 mm and EQ69 mm LVWTs were identified as independent predictors of arrhythmic events, over and above the conventional risk stratification model.

**Study Limitations**

Few limitations apply to our study. Annual Holter monitoring may have captured only a limited amount of NSVTs in the VAEs population. Similarly, VAEs may have been present but not captured, even with 48-h Holter monitoring, in the patients that we have assigned to be event-free. Despite the rigorous protocol and its consistent application in this study population, it may provide only an excerpt of the arrhythmic burden. Although this study did not attempt to test the role of NSVT in relation to SCD in HCM, future studies are needed to improve understanding of associated risk, if any.

**Conclusions**

Non-invasive imaging measures, such as LVWT, do have a role in identifying the high-risk patients with HCM. Maximum LVWT provides valuable information, but only as part of an overall risk stratification model. Regional LVWT of key segments plays an independent role in the prediction of arrhythmic events.

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**Disclosures**

Authors report no conflicts of interest.

**References**


