Comparison between maximal left ventricular wall thickness and left ventricular mass in patients with hypertrophic cardiomyopathy

Mateusz Śpiewak1,2, Lidia Chojnowska3, Łukasz A. Malek2,3, Barbara Milosz2,4, Joanna Petryka1,2, Magdalena Żabicka2,4, Mariusz Klopotowski3, Maciej Dąbrowski3, Jolanta Miśko2,4, Witold Rużyłło5

1Department of Coronary Artery Disease and Structural Heart Diseases, Institute of Cardiology, Warsaw, Poland
2Magnetic Resonance Unit, Institute of Cardiology, Warsaw, Poland
3Department of Cardiology and Interventional Angiology, Institute of Cardiology, Warsaw, Poland
4Department of Radiology, Institute of Cardiology, Warsaw, Poland
5Institute of Cardiology, Warsaw, Poland

Abstract

Background: Cardiovascular magnetic resonance enables accurate and reproducible assessment of left ventricular (LV) dimensions and function, free of geometric assumptions and limitations related to an inadequate acoustic window. In patients with hypertrophic cardiomyopathy (HCM), LV mass (LVM) and maximal LV wall thickness (MLVWT) have prognostic significance.

Aim: To compare MLVWT and LVM in patients with HCM.

Methods: The study population included 33 patients with HCM (17 males, mean age 48.5 ± 16.5 years). Subjects after alcohol septal ablation or surgical myectomy were excluded from the study. The MLVWT and LVM were measured with the use of cardiac magnetic resonance. The MLVWT was determined with the use of the dedicated software in short axis slices after manual definition of endocardial and epicardial contours. The LVM was indexed for body surface area and expressed in g/m². Cut-off values for normal, mildly increased and markedly increased LVM were based on previously published studies.

Results: Mean LVM in the whole study group was 107.4 ± 30.9 g/m² (range 57.0–163.4 g/m²) and was higher in males than females (120.2 ± 30.8 g/m² vs 93.8 ± 25.3 g/m², respectively; p = 0.01). Mean MLVWT was 23.4 ± 4.8 mm (range 16–36 mm). There was only a weak trend toward higher MLVWT in men when compared to women (24.8 ± 5.4 mm vs 21.9 ± 3.7 mm, respectively; p = 0.09). There was no correlation between LVM and MLVWT (r = 0.24; p = 0.17). A significant variability in LVM was observed in subjects with similar MLVWT; a greater than two-fold difference was noted in extreme cases. In three patients (9%; one female, two males) LVM was within the normal range and in another one female (3%) patient LVM was mildly increased. In the remaining patients (n = 29; 88%) markedly increased LVM was observed.

Conclusions: The MLVWT does not reflect the degree of LV hypertrophy in patients with HCM. Patients with similar MLVWT may have substantial differences in LVM. A substantial group of patients with HCM is characterised by normal, or only mildly increased LVM, despite significant LV wall hypertrophy measured as MLVWT.

Key words: hypertrophic cardiomyopathy, cardiac magnetic resonance, left ventricular mass
INTRODUCTION
Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiac disorder, affecting about 1 in 500 of the general adult population [1]. The diagnostic criteria are an otherwise unexplained maximal left ventricular (LV) wall thickness (MLVWT) $\geq 15$ mm [1] associated with a non-dilated ventricular cavity. Massive LV hypertrophy expressed as MLVWT greater or equal to 30 mm is one of the major risk factors for sudden cardiac death (SCD) in patients with HCM [1]. Cardiovascular magnetic resonance (CMR) enables accurate and reproducible assessment of LV dimensions and function, free of geometric assumptions and limitations related to an inadequate acoustic window. Maron et al. [2] showed that in patients with HCM, CMR gives additional information when compared to transthoracic echocardiography, enabling precise assessment of the anterolateral wall, posterior septum and apex. Moreover, CMR proved to be superior to echocardiography in detecting LV hypertrophy, and therefore in diagnosis of HCM [3]. It has been demonstrated that 21% of patients with HCM have normal LV mass (LVM) and that HCM without markedly increased LVM carries an excellent prognosis [4].

The aim of the current study was to compare LVM and MLVWT in a subset of patients from a large Polish cohort of HCM patients.

METHODS

Patient population
The study population has been described in detail previously [5]. Briefly, the study included 33 consecutive patients with HCM referred for CMR as a part of routine medical assessment. Patients after surgical myectomy or alcohol septal ablation were excluded from the study. Diagnosis of HCM was based on the MLVWT $\geq 15$ mm (without concomitant LV dilatation) in the absence of other causes capable of producing a similar amount of hypertrophy [1].

The study was approved by the local research ethics committee; all patients (and/or parents/guardians when needed) gave written informed consent.

CMR study
All studies were performed on a 1.5 T scanner (Avanto, Siemens, Erlangen, Germany) as previously described [5, 6]. In brief, after scout images, ECG-gated breath-hold steady state free precession (SSFP) cine images were acquired in LV long axis (2-, 3- and 4-chamber views). In addition, a stack of short axis slices covering both ventricles from base to apex was obtained.

Data analysis
After manual contouring epicardial and endocardial borders at end-diastole and end-systole left ventricular end-diastolic and end-systolic volumes (LVEDV and LVESV, respectively) and LVM were calculated with the use of commercially available software (Mass 6.2.1, Medis, Leiden, the Netherlands). Left ventricular mass was calculated by multiplying LV myocardium volume by 1.05 g/mL. Maximal LV wall thickness was determined by MASS software as the maximal distance between endocardial and epicardial contour on short axis slices. Papillary muscles were not included in LVM [4, 7]. The LVEDV, LVESV and LVM were indexed for body surface area and expressed in ml/m² or g/m², respectively.

Reference values for LVM for males and females were taken from the Framingham study cohort including 606 patients (239 men, 367 women) [7]. Normal LVM [($\leq $ mean $+ +$ 2 standard deviations (SD)) was defined as LVM $< 62$ g/m² for females and LVM $< 81$ g/m² for males. Mildly (mean $+ +$ 2 SD) and markedly increased (mean $+ +$ 3 SD) were: 62–69 g/m² and $> 69$ g/m² for women and 81–91 g/m² and $> 91$ g/m² for men, respectively [4].

Statistical analysis
Data are presented as numbers and percentages or means $\pm$ SD, unless otherwise specified. Variables were tested for normality using the Kolmogorov-Smirnov test. Correlations were assessed using Pearson’s correlation coefficient. A p value $< 0.05$ was considered to denote a statistically significant difference. All statistical testing was performed using MedCalc 10.0.2.0 statistical software (MedCalc, Mariakerke, Belgium).

RESULTS
In all patients, quality of images enabled analysis of the studied parameters. As previously reported, in one patient scanning was interrupted due to dyspnea [5]. However, SSFP images of all short axis slices were acquired before termination of the study and the patient was included in the current analysis.

Cardiovascular magnetic resonance parameters of the study population [17 males (53%), mean age 48.5 $\pm +$ 16.5 years (range 14–75)] are shown in Table 1. Figure 1 demonstrates representative images of MLVWT measurement with the use of dedicated software. Mean LVM was 107.4 $\pm +$ 30.9 g/m² (range 57.0–163.4) and was higher in males than in females (120.2 $\pm +$ 30.8 vs 93.8 $\pm +$ 25.3 g/m², respectively;
Comparison between MLVWT and LVM in patients with HCM

With the use of pre-specified cut-off values, it was demonstrated that one female patient and two male patients had LVM within the normal range (Fig. 4). The highest MLVWT in this subgroup was 23 mm. Overall, in the whole group 9% patients had normal LVM. Additionally, in one female patient LVM was mildly increased. Markedly increased LVM was present in 29 (88%) patients.

There were four patients (three men, one woman; 12%) with LVMWT ≥ 30 mm. All four had markedly increased LVM (mean 104.1 ± 19.1 g/m², range 92.0–132.5).

DISCUSSION

Our study demonstrated that LVM varies greatly among patients with a similar degree of LV wall hypertrophy. This confirmed the results of a previous study [4]. Moreover, we showed that 9% of patients had normal LVM despite severe regional hypertrophy expressed as MLVWT. This number is lower than reported by Olivotto et al. [4]. This discrepancy can be explained by differences in baseline characteristics of patients, including slightly higher mean LVM and mean MLVWT in our study. Nevertheless, results of a previous multicentre trial [4] and current analysis indicate that there is a substantial group of HCM patients with LVM within the normal range. The incidence of this phenomenon varies in different populations.

Cardiac magnetic resonance in patients with HCM is increasingly being recognised as a robust diagnostic and pro-

---

**Figure 1.** Representative images demonstrating how maximal left ventricular wall thickness (MLVWT) is calculated; A. Short axis slice after manual contouring of endocardial and epicardial borders; B. MLVWT calculated by software using the centreline method.

**Figure 2.** Correlation between left ventricular mass (LVM) and maximal left ventricular wall thickness (MLVWT) (r = 0.24, p = 0.17). Open circles represent women and dark circles represent men. Solid line indicates the upper limit of normal range in males, and dashed line in females. Note the significant differences in LVM in patients with similar MLVWT, especially when males and females are compared.
CMR enables identification of areas of late gadolinium enhancement (LGE), which correspond to areas of myocardial fibrosis [8] and may have prognostic information regarding the frequency and occurrence of arrhythmias and SCD risk [9, 10]. Also, other studies provide evidence for an association between LGE and ventricular arrhythmias [11–13]. Nevertheless, the clinical value of comprehensive assessment, including LGE analysis as well as LVM, is not completely understood. Both MLVWT and LGE have been shown to be independent predictors of SCD risk [10]. Moon et al. [14] demonstrated a greater extent of LGE in patients with ≥ 2 risk factors for SCD including MLVWT ≥ 30 mm. The study by Maron et al. [15] showed that patients with LGE had both larger MLVWT and LVM when compared to individuals with no evidence of hyperenhancement. It has also been proved that increased maximal septal thickness is an independent predictor of positive LGE [13]. On the other hand, the observations of Petkow-Dimitrov et al. [11, 16] indicate no differences in LVM and MLVWT between patients with and without ventricular arrhythmias despite a higher incidence of LGE in patients with non-sustained ventricular tachycardia [11].

Apart from calculations of LVM and MLVWT, CMR enables accurate and reproducible measurement of ventricular volume and ejection fraction free of geometrical assumptions and a poor acoustic window. Moreover, CMR helps in differential diagnosis of doubtful cases [17, 18]. Taking into consideration the results of the study by Olivotto et al. [4] showing no HCM-related mortality in patients without markedly elevated LVM, the present study may indicate the ability of CMR in identifying patients at low risk of death in mid-term follow-up. This may have an impact on the currently used risk stratification model in this population and indications for cardioverter-defibrillator implantation. This issue requires further investigation.

**Limitations of the study**

The major limitation of our study is its small sample size that did not allow us to perform detailed analyses of subgroups (e.g. compare patients at different risks of SCD).
However, this was not the purpose of the study. Moreover, we did not assess the relationship between CMR parameters and echocardiographic data. Nevertheless, a recent study provides evidence for high agreement between MLVWT assessed by echocardiography and CMR [4]. Moreover, new echocardiographic techniques such as real-time three-dimensional echocardiography showed excellent agreement with CMR reference in LVM and MLVWT measurements [19].

CONCLUSIONS
In conclusion, MLVWT does not reflect the degree of LV hypertrophy in patients with HCM. Patients with the same MLVWT may have substantial differences in LVM. A substantial group of patients with HCM is characterised by normal, or only mildly increased, LVM.

References
Streszczenie

Wstęp: Rezonans magnetyczny serca umożliwia wiarygodną i powtarzalną ocenę wielkości i funkcji lewej komory, niezależną od geometrycznych przybliżeń oraz nieodpowiedniej jakości okna akustycznego. U pacjentów z kardiomiopatią przerostową (HCM) masa lewej komory (LVM) i maksymalna grubość ściany lewej komory (MLVWT) mają znaczenie rokownicze.

Cel: Celem pracy było porównanie MLVWT z LVM u pacjentów z HCM.

Metody: Badaną grupę stanowiło 33 chorych z HCM (17 mężczyzn, średni wiek 48,5 ± 16,5 roku). Z badania wyłączono osoby po ablacji alkoholowej przegrody lub chirurgicznej miektomii w wywiadzie. Oceny MLVWT i LVM dokonywano przy użyciu badania serca metodą rezonansu magnetycznego, natomiast MLVWT mierzył automatycznie program komputerowy na przekrojach w osi krótkiej po ręcznym obrysowaniu konturów wsierdzia i nasierdzia. Masę lewej komory indeksowano na powierzchnię ciała i wyrażono w g/m². Punkty odcięcia dla poszczególnych kategorii LVM (prawidłowa, nieznacznie zwiększona, znacznie zwiększona) określono na podstawie wcześniej opublikowanych badań.

Wyniki: Średnia LVM w całej grupie wynosiła 107,4 ± 30,9 g/m² (zakres 57,0–163,4 g/m²) i była wyższa u mężczyzn niż u kobiet (odpowiednio 120,2 ± 30,8 g/m² v. 93,8 ± 25,3 g/m²; p = 0,01). Wartość MLVWT wynosiła średnio 23,4 ± 4,8 mm (zakres 16–36 mm). Wykazano jedynie słaby trend w kierunku większej MLVWT u mężczyzn niż u kobiet (odpowiednio 24,8 ± 5,4 mm v. 21,9 ± 3,7 mm; p = 0,09). Wartości MLVWT i LVM nie korelowały ze sobą (r = 0,24; p = 0,17). Zaobserwowano znaczne różnice w LVM u pacjentów z podobną MLVWT. W skrajnych przypadkach LVM różniła się ponad 2-krotnie; LVM znajdowała się w granicach normy u 3 osób (9%; 1 kobieta, 2 mężczyzn), a u 1 pacjentki (3%) była nieznacznie podwyższona. U pozostałych chorych (n = 29; 88%) LVM była istotnie zwiększona.

Wnioski: Maksymalna grubość ściany lewej komory nie odzwierciedla w pełni stopnia przerostu mięśnia lewej komory u chorych z HCM. U pacjentów z tą samą MLVWT mogą występować znaczne różnice w zakresie LVM. U części chorych z HCM stwierdza się prawidłową lub jedynie nieznacznie zwiększoną LVM mimo obecności istotnego przerostu ścian lewej komory.

Słowa kluczowe: kardiomiopatia przerostowa, rezonans magnetyczny serca, masa lewej komory

Kardiol Pol 2010; 68, 7: 763–768

Adres do korespondencji:
lek. Mateusz Śpiewak, Klinika Choroby Wieńcowej i Strukturalnych Chorób Serca, Instytut Kardiologii, ul. Alpejska 42, 04–628 Warszawa, e-mail: mspiewak@ikard.pl

www.kardiologiapolska.pl