Assessment of Cardiac Dimensions in Children Diagnosed with Hypertrophic Cardiomyopathy

Kaushiki Bakaya[a,*] (BSc, Med), Waleed Paracha[a,*] (BSc, Med), Silvia Schievano[b] (PhD), Selim Bozkurt[b,c] (PhD)

[a] UCL Medical School, University College London, London, United Kingdom

[b] Institute of Cardiovascular Science, University College London, London, United Kingdom

[c] School of Engineering, Ulster University, Newtownabbey, United Kingdom

[*] K.B. and W.P contributed equally to this article and are the joint first authors

Correspondence: Selim Bozkurt

e-mail: s.bozkurt1@ulster.ac.uk

Statements

Data Availability: Data analysed during this study are included in the article.

Funding: This research received no external funding.

Institutional Review Board Statement: Data was analysed in accordance with the guidelines laid out in the Declaration of Helsinki. Ethical approval was obtained for the use of image data for research purposes (UK REC 06/Q0508/124) from the Joint Research and Development Office of Great Ormond Street Hospital for Children.

Informed Consent Statement: All parents/guardians gave written informed consent to participate in this study.

Conflicts of Interest: The authors declare no conflict of interest.

Abstract

Background: Hypertrophic cardiomyopathy (HCM) is an inherited autosomal dominant heart disease, characterised by increased left ventricular wall thickness and abnormal loading conditions. Imaging modalities are the first choice for diagnosis and risk stratification. Although heart dimensions have been characterised widely in HCM adults from cardiac imaging, there is limited information about children affected by HCM. The aim of this study is to evaluate left ventricular function and left heart dimensions in a small population of children diagnosed with HCM.

Methods: A total of 16 (7 male, 9 female) paediatric patients with an average age of 14.0±2.5 years diagnosed with HCM at Great Ormond Street Hospital for Children were included in this study. Cardiac magnetic resonance images were used to measure left and right ventricular dimensions, and septal and left ventricular free wall thicknesses in Simpleware ScanIP. The gender groups were compared using student t-test or non-parametric Mann-Whitney U test depending on the sample distribution.

Results: Differences in heart rate, left ventricular end-diastolic volume and end-diastolic volume index, left ventricular stroke volume and stroke volume index, left ventricular end-systolic long axis length, left ventricular end-systolic long axis length index, left ventricular end-diastolic mid-cavity diameter, left ventricular end-diastolic free wall thickness, left ventricular end-diastolic free wall thickness index, right ventricular end-diastolic long axis length were statistically significant in males and females.

Conclusion: Left ventricular wall and intraventricular septal thickness increase affecting left ventricle cavity dimensions and there may be differences in anatomical and physiological parameters in males and females affected by HCM.

Keywords: hypertrophic cardiomyopathy; paediatric patients; cardiac magnetic resonance imaging

Introduction

Hypertrophic cardiomyopathy (HCM) is an inherited, autosomal dominant primary heart disease, characterised by increased left ventricular wall thickness without ventricle dilation **[1]**. In the adult population, it is a common genetic cardiovascular disease, affecting 1 in 500 people with increasing diagnosis rate after 40 years of age; however, it has a much lower prevalence in children, where it only affects 0.47 children per 100,000 **[2–4]**.

HCM is often associated with left ventricular diastolic dysfunction– reduced ability of the left ventricle to relax fully. This translated in reduced left ventricular filling and, therefore, reduced cardiac output **[5]**. Histological evidence shows myocardial fibre disarray and fibrosis in HCM samples, often with short runs of severely hypertrophied fibres, especially in the septal tissue **[6]**. Therefore, HCM-affected hearts produce lower strength per muscle cross-sectional area compared to healthy hearts.

In paediatrics, the cause of HCM is generally mutations in various genes, especially those associated with sarcomeres, intercellular calcium modulators or z-discs such as MYBPC3 or MYH7 **[7]**. HCM patients have been found to have a significantly greater indexed LV mass and wall thickness compared to healthy subjects. The extent and distribution of LV hypertrophy in paediatric patients vary considerably due to diverse genetic and molecular causes and concomitant conditions such as arterial hypertension or aortic stenosis **[1,8]**. For instance, left ventricular mass index and maximal left ventricular wall thickness indices may reach up to 101.4 g/m^2 and 19.6 mm/m^2 whereas these variables are around 35.9 g/m^2 and 5.7 mm/m^2 in normal children around 13 years old **[9]**. In childhood, HCM often occurs alongside left ventricular outflow tract obstruction and mitral regurgitation **[10,11]**. These are most commonly the result of increased myocardial hypertrophy, with subsequent anterior motion of the anterior mitral leaflet and subvalvular apparatus during systole **[11,12]**. Usually, obstructive HCM in children is linked with substantial thickening of the anterior basal septum opposite to the anterior leaflet of the mitral valve **[4]**.

Cardiac imaging modalities such as echocardiography, magnetic resonance imaging or nuclear imaging and computerised tomography are used as diagnostic tools to identify the morphologic and functional changes in patients **[13]**. HCM is diagnosed measuring left ventricular diastolic septal thickness and free wall thickness. Suggested diagnostic criteria for HCM defined using a z-score which shows how many standard deviations below or above the population mean and z-score two times higher than healthy population shows existence of HCM **[5,13,14]**. However, use of z-score two times higher than healthy population is criticised because left ventricular wall is too sensitive in children when compared to adults **[15]**. Therefore, diagnostics criteria remain non-established in children and recent guidelines suggest that a maximal wall thickness that with a z-score ≥20 whilst >10 can be used

with combination of different risk factors **[16]**. Although in adults information about the diagnosis and risk stratification of HCM is well established, there is limited data on the cardiac function and heart chamber dimensions in children **[9]**. Sahin et al. **[17]** investigated clinical characteristics of paediatric patients diagnosed with HCM in syndromic and non-syndromic patients. They concluded that the morphological, functional, and clinical features of HCM in children are heterogeneous and highly depends on the cause and age. Wang and Zhu **[18]** reviewed clinical characteristics of paediatric patients affected by HCM and concluded that novel prognostic markers are needed to predict sudden cardiac death in children with HCM. El Assaad et al. **[19]** utilised exercise stress echocardiography to evaluate clinical characteristics of HCM in children at rest and exercise and concluded exercise stress echocardiography can be used in children with HCM as risk-stratifying tool. Windram et al. **[20]** compared myocardial dimensions measured with echocardiography and magnetic resonance imaging finding that magnetic resonance imaging is more reliable than echocardiography to measure circumferential myocardial thickness. As there is limited data available about HCM in children, z-scores ranges for children in HCM have not been defined yet, therefore, adult z-score thresholds are recommended as diagnostic criteria in paediatric patients **[5]**. Therefore, investigating cardiac dimension ranges in children diagnosed with HCM will help to establish better diagnostic criteria for paediatric patients. The aim of this study is to investigate anatomical and haemodynamic characteristics in children diagnosed with HCM along with comparing the anatomical and haemodynamic characteristics in male and female patients.

Materials and Methods

A total of 16 (7 male, 9 female, 14.0 ± 2.5 [10-17] years old) paediatric patients diagnosed with HCM at Great Ormond Street Hospital for Children, London were included in this study. The average age for male patients was 13.9 ± 3.4 years ranging between 7 and 17 years, whilst for females was 14.1 ± 1.8 years, ranging between 11 and 16 years.

Patient demographics and hemodynamic parameters were collected from the hospital database: age, gender, height, weight, body mass index, heart rate, end-diastolic and end-systolic volumes, end-diastolic and end-diastolic volume indices, left ventricular ejection fraction, cardiac output, cardiac index and left ventricular mass index. Cardiac magnetic resonance (CMR) images (1.5-Tesla Magnetom Avanto scanner, Siemens Medical Solutions, Erlangen, Germany) were reviewed for this study. The steady-state free precession (SSFP) sequences, displaying relatively high blood to muscle contrast compared to other CMR sequences, allowed ventricular measurement **[21]**, acquired at both end-diastole, and end-systole, each identified as the point of the cardiac cycle with the largest and smallest left ventricular cavity size, respectively. Four-chamber and short-axis views were used to measure left

ventricular long axis length, left ventricular mid-cavity diameter, right ventricular long axis length, right ventricular mid-cavity diameter, intraventricular septal thickness, left ventricular lateral septal diameter and left ventricular free wall thickness at the end of diastolic and systolic phases using the image segmentation and processing software Simpleware ScanIP 2018 (Synopsis, CA, USA) as given in Figure 1.

The measurements from the two groups (male vs. female) were statistically compared using student t-test or non-parametric Mann-Whitney U test depending on the sample distribution evaluated utilising the Shapiro-Wilk test **[22]** (IBM SPSS 27, Armonk, New York, USA). P-values <0.05 were assumed to be statistically significant.

Reproducibility of the measurements was assessed in four randomly selected subjects. Intra-class correlation coefficients (ICC) with 95% confidence interval were calculated to assess the inter and intra observer variability using MedCalc 19.7 (MedCalc, Ostend, Belgium). Inter-observer reproducibility analysis was done using one-way random effects model to evaluate randomly selected observers for each subject. Intra-observer variability analysis was done utilising two-way model to evaluate the same observer for the selected measurements.

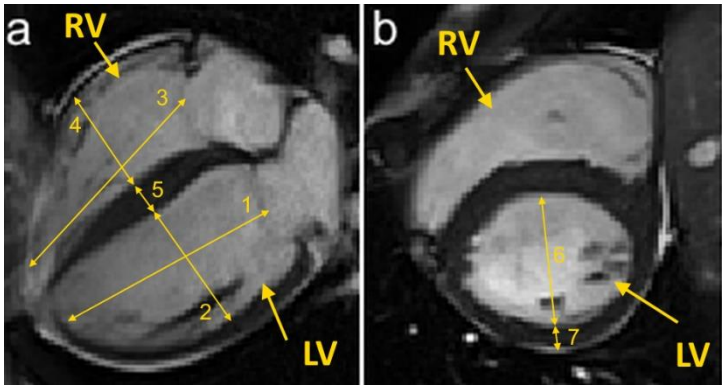

Figure 1. Heart chamber and wall dimensions measured on the cardiac magnetic images. 1. left ventricular long axis length, 2. left ventricular mid-cavity diameter, 3. right ventricular long axis length, 4. right ventricular mid-cavity diameter, 5. intraventricular septal thickness, 6. left ventricular lateral septal diameter, 7. left ventricular free wall thickness, (LV and RV represent left and right ventricles).

Results

Average values and standard deviations of the patient characteristics and haemodynamic variables in left ventricle and p-values for the statistical comparison between the groups are given in Table 1.

Table 1. Average values and standard deviations of the patient data and haemodynamics, superscript *n* represents non-parametric statistical comparison, * shows the statistically significant differences between the groups. (LV represents left ventricle).

	All patients	**Male**	**Female**	**p-values**
Age [years]	14.0 ± 2.5	13.9 ± 3.4	14.1 ± 1.8	0.861
Body Surface Area [m^2]	1.58 ± 0.30	1.65 ± 0.34	1.52 ± 0.26	0.395
Height [m]	1.62 ± 0.14	1.67 ± 0.17	1.59 ± 0.10	0.252^n
Weight [kg]	55.68 ± 18.06	59.16 ± 17.76	52.97 ± 18.87	0.512
Body Mass Index [kg/m^2]	20.65 ± 4.94	20.60 ± 3.24	20.70 ± 6.15	0.606^n
Heart Rate [bpm]	68.19 ± 13.02	59.14 ± 6.20	75.22 ± 12.73	0.006*
End-diastolic LV Volume [mL]	115.25 ± 33.23	141.57 ± 31.30	94.78 ± 16.06	0.006*
End-diastolic LV Volume Index [mL/m^2]	73.44 ± 17.20	86.57 ± 15.43	63.22 ± 10.40	0.006*
End-systolic LV Volume [mL]	34.56 ± 16.04	43.86 ± 19.02	27.33 ± 8.76	0.066
End-systolic LV Volume Index [mL/m^2]	22.06 ± 9.40	27.00 ± 11.31	18.22 ± 5.63	0.096
LV Stroke Volume [mL]	80.69 ± 21.38	97.71 ± 20.62	67.44 ± 9.34	0.007*
LV Stroke Volume Index [mL/m^2]	51.39 ± 10.30	59.58 ± 8.97	45.02 ± 5.85	0.004*
LV Ejection Fraction [%]	70.63 ± 7.09	69.29 ± 8.92	71.67 ± 5.63	0.552
Cardiac Output [L/min]	5.37 ± 1.13	5.79 ± 1.29	5.04 ± 0.93	0.091^n
Cardiac Index [$L/min/m^2$]	3.45 ± 0.72	3.50 ± 0.53	3.41 ± 0.87	0.806
LV Mass Index [g/m^2]	79.93 ± 16.38	87.79 ± 14.48	73.82 ± 15.81	0.088
E/A Ratio	1.57 ± 0.12	1.53 ± 0.52	1.63 ± 0.34	<0.001*

Average body surface area of the cohort was 1.58 m^2, height was 1.62 m and weight was 55.68 kg. Although the males had higher average body surface area, height and weight than the females, there was no significant difference between the two groups. Average body mass index of all patients was 20.65 kg/m^2, with male and female patients presenting similar values. There was a significant difference in the heart rate between male and female patients. Average left ventricular end-diastolic volume, and end-diastolic volume index were significantly higher in the male patients. Although there was a difference for the average left ventricular end-systolic volume and end-systolic volume index between the groups, this was not statistically significant. Left ventricular stroke volume and stroke volume index were significantly different between the male and female patients.

Average left ventricular ejection fraction was similar for males and females. Average cardiac output for the cohort was 5.37 L/min. Although there was a relatively high cardiac output in the male patients, the difference in the cardiac output for females and males was not statistically significant. Also, cardiac index was similar in both groups. Average left ventricular mass index was no significantly different in male and female patients. E/A ratio was significantly different in male and female patients. Average values and standard deviations of the left and right ventricular dimensions and p-values for the statistical comparison between the groups are given in Table 2. Available CMR images from the patients are given as supplementary material.

Table 2. Average values and standard deviations of the left and right ventricular dimensions, superscript *n* represents non-parametric statistical comparison, * shows the statistically significant differences between the groups. (LV, RV and IV represent left and right ventricle and intraventricular respectively)

	All patients	**Male**	**Female**	**p-values**
LV end-diastolic lateral septal diameter [mm]	43.58 ± 5.28	46.16 ± 5.35	41.57 ± 4.52	0.094
LV end-diastolic lateral septal diameter index [mm/m^2]	28.33 ± 5.26	28.96 ± 6.92	27.85 ± 3.90	0.713
LV end-systolic lateral septal diameter [mm]	22.59 ± 5.96	24.67 ± 6.36	20.98 ± 5.44	0.681^n
LV end-systolic lateral septal diameter index [mm/m^2]	14.62 ± 3.92	15.31 ± 4.00	14.08 ± 4.01	0.554
LV end-diastolic long axis length [mm]	84.13 ± 12.06	92.56 ± 12.65	77.57 ± 6.49	0.020*
LV end-diastolic long axis length index [mm/m^2]	54.42 ±8.39	57.07 ± 7.57	52.35 ± 8.84	0.270
LV end-systolic long axis length [mm]	61.43 ± 18.31	74.31 ± 10.01	51.4 ± 17.18	0.005*
LV end-systolic long axis length index [mm/m^2]	39.25 ± 11.34	45.98 ± 7.43	34.02 ± 11.36	0.024*
RV end-diastolic long axis length [mm]	61.70 ± 17.18	72.94 ± 18.05	52.96 ± 10.59	0.028*
RV end-diastolic long axis length index [mm/m^2]	39.89 ± 11.67	45.84 ± 14.12	35.27 ± 7.11	0.106
RV end-systolic long axis length [mm]	38.89 ± 11.81	44.87 ± 12.11	34.23 ± 9.80	0.084
RV end-systolic long axis length index [mm/m^2]	24.98 ± 7.25	27.76 ± 7.40	22.82 ± 6.74	0.114^n
LV end-diastolic mid-cavity diameter [mm]	41.78 ± 7.21	46.86 ± 3.69	37.83 ± 6.86	0.005*
LV end-diastolic mid-cavity diameter index [mm/m^2]	27.06 ± 5.59	29.40 ± 6.58	25.23 ± 4.19	0.175
LV end-systolic mid-cavity diameter [mm]	20.56 ± 5.17	22.49 ± 4.89	19.06 ± 5.13	0.196
LV end-systolic mid-cavity diameter index [mm/m^2]	13.51 ± 4.38	14.39 ± 5.18	12.82 ± 3.82	0.516
RV end-diastolic mid-cavity diameter [mm]	34.24 ± 5.84	36.64 ± 3.32	32.38 ± 6.83	0.127
RV end-diastolic mid-cavity diameter index [mm/m^2]	22.09 ± 4.46	23.11 ± 6.18	21.30 ± 2.65	0.606^n
RV end-systolic mid-cavity diameter [mm]	17.2 ± 5.43	18.84 ± 4.59	15.93 ± 5.95	0.351^n
RV end-systolic mid-cavity diameter index [mm/m^2]	11.15 ± 3.99	12.00 ± 4.74	10.49 ± 3.44	0.492
LV end-diastolic free wall thickness [mm]	7.81 ± 1.64	9.27 ± 1.09	6.68 ± 0.93	<0.001*
LV end-diastolic free wall thickness index [mm/m^2]	5.05 ± 1.16	5.82 ± 1.36	4.45 ± 0.47	0.037*
LV end-systolic free wall thickness [mm]	16.21 ± 3.96	17.24 ± 3.52	15.40 ± 4.30	0.362
LV end-systolic free wall thickness index [mm/m^2]	10.63 ± 3.66	11.01 ± 4.52	10.33 ± 3.09	0.606^n
IV end-diastolic septal thickness [mm]	17.24 ± 5.11	16.86 ± 5.61	17.54 ± 5.02	0.803
IV end-diastolic septal thickness index [mm/m^2]	11.16 ± 3.40	10.22 ± 2.51	11.89 ± 3.94	0.536^n
IV end-systolic septal thickness [mm]	21.99 ± 6.00	23.06 ± 5.68	21.16 ± 6.44	0.470^n
IV end-systolic septal thickness index [mm/m^2]	14.15 ± 3.64	13.99 ± 2.09	14.28 ± 4.63	0.870

Although there was a high difference in the left ventricular end-diastolic lateral septal diameter between the groups, this difference was not statistically different. Average left ventricular end-diastolic lateral septal diameter index was similar for both groups. Left ventricular end-systolic lateral septal diameter and left ventricular end-systolic lateral septal diameter index were also similar in both groups.

There was a significant difference in left ventricular end-diastolic long axis length between the male and female patients. However, the difference in the left ventricular end-diastolic long axis length index between the groups was not statistically significant. Average left ventricular end-systolic long axis length, and end-systolic long axis length index were significantly different in male and female patients.

Although the difference in the right ventricular end-diastolic long axis length for male and females were statistically significant, there was no statistical significance for the right ventricular end-diastolic long axis length index. There was no significant difference for the groups in average right ventricular end-systolic long axis length. Similarly, the right ventricular end-systolic long axis length index was not statistically significant either for both groups.

Although there was a significant difference between male and female patients for the left ventricular end-diastolic mid-cavity diameter, indexed left ventricular end-diastolic mid-cavity diameter was not statistically different in both groups. Also left ventricular end-systolic mid cavity diameter and end-systolic mid cavity diameter index were not statistically different.

There was no significant difference between the groups in average right ventricular end-diastolic mid-cavity diameter, end-diastolic mid-cavity diameter index, end-systolic mid-cavity diameter and end-systolic mid-cavity diameter index.

There was a significant difference between the male and female patients in left ventricular end-diastolic free wall thickness and end-diastolic free wall thickness index whereas end-systolic free wall thickness and end-systolic free wall thickness index were similar in both groups.

There was no statistical significance between the groups for average end-diastolic septal thickness, end-diastolic septal thickness index, end-systolic septal thickness and indexed end-systolic septal thickness. ICC and 95% intervals for the reproducibility of the measurements are given in Table 3.

Table 3. Reproducibility for the measurements. (ICC represents intra-class correlation coefficient, LV, RV and IV represent left and right ventricle and intraventricular respectively)

	Inter-observer		Intra-observer	
	ICC	**95% interval**	**ICC**	**95% interval**
LV end-diastolic lateral septal diameter	0,99	0,96 - 0,99	0,99	0,61 - 0,99
LV end-systolic lateral septal diameter	0,98	0,93 - 0,99	0,99	0,70 - 0,99
LV end-diastolic long axis length	0,95	0,75 - 0,99	0,98	0,47 - 0,99
LV end-systolic long axis length	0,98	0,91 - 0,99	0,97	0,58 - 0,99
RV end-diastolic long axis length index	0,98	0,88 - 0,99	0,99	0,86 - 0,99
RV end-systolic long axis length	0,89	0,42 - 0,99	0,99	0,95 - 0,99
LV end-diastolic mid-cavity diameter	0,99	0,97 - 0,99	0,99	0,99 - 1,00
LV end-systolic mid-cavity diameter	0,84	0,16 - 0,99	0,98	0,86 - 0,99
RV end-diastolic mid-cavity diameter	0,99	0,93 - 0,99	0,98	0,79 - 0,99
RV end-systolic mid-cavity diameter	0,86	0,26 -0,99	0,92	-0,38 - 0,99
LV end-diastolic free wall thickness	0,48	-1,77 - 0,96	0,81	-0,57 - 0,99
LV end-systolic free wall thickness	0,83	0,11 - 0,99	0,96	0,48 - 0,99
IV end-diastolic septal thickness	0,99	0,99 - 0,99	0,99	0,98 - 0,99
IV end-systolic septal thickness	0,98	0,88 - 0,99	0,99	0,58 - 0,99

ICC values were above 0.80 except in the inter-observer left ventricular analysis for the end-diastolic free wall thickness. High ICC values show reproducible and consistent measurements.

Discussion/Conclusion

In this study, we investigated dimensions of the left and right ventricles and left ventricular wall and septum in children diagnosed with HCM. Cardiac dimensions such as long axis length mid cavity diameter, free wall thickness in the left ventricle or intraventricular septal thickness together with right ventricular dimensions have been reported in this study. Therefore, findings in this study provides information not only about the ventricular wall dimensions but also how the ventricular cavity is influenced by HCM. We also compared ventricular and wall dimensions in male and female patients using statistical analyses. Previously, Chaowu et al. [9] reported cardiac magnetic resonance characteristics in children diagnosed with HCM. Patient characteristics such as age and body surface area in [9] were similar to the patients' age and body surface area in this study. Moreover, left

ventricular end-diastolic and end-systolic volumes, left ventricular end-diastolic, and end-systolic volume indexes and cardiac index of the patients were similar as well. Therefore, the findings about the left ventricular size in this study confirm the findings in [9]. There was a statistically significant difference in body surface area of the male and female patients in Chaowu et al. [9] whereas in this study age and body surface area of the male and female patients was not significantly different. Statistical comparison in [9] showed that left ventricular mass and mass index, left ventricular maximal wall thickness and left ventricular end-systolic volume index were significantly different for male and female patients. In our study, there was not statistical significance in these variables between males and females. This might be because the body surface area of the males and females were significantly different in Chaowu et al. [9]. In this study, heart rate, left ventricular end-diastolic volume and volume index, left ventricular stroke volume and stroke volume index, left ventricular end-diastolic and end-systolic long axis lengths, left ventricular end-systolic long axis index, right ventricular end-diastolic long axis length, left ventricular end-diastolic mid-cavity diameter, left ventricular end-diastolic free wall thickness and free wall thickness index were significantly different in male and female patients. Intraventricular septal thickness is around 6 mm in children at 6 years old [23], and it reaches around 8 mm after 20 years of age [24]. Average intraventricular septal thickness was around 17 mm at the end of diastole and 14 mm at the end of systole in the children diagnosed with HCM (Table 2). Left ventricular diastolic free wall thickness is around 7 mm, and systolic wall thickness is around 10 mm at 10 years of age [25]. It changes within a similar range at the year of age as well [24]. The findings in this study shows that left ventricular wall thickness was almost doubled in children with HCM (Table 2).

Average left ventricular long axis length in healthy children is around 9 mm at the diastole and 8 mm at the systole in the children with 1.6 m^2 body surface area [26]. In this study, left ventricular end-diastolic long axis length of the cohort was around 84 mm whereas the end-systolic length of the left ventricle around 61 mm. HCM can present itself in different phenotypes and result in a reduction of left ventricular cavity size [27,28]. Reduced lateral-septal and mid-cavity diameters in the patients also confirm this when compared with healthy values [29].

E/A ratio which can be used to evaluate ventricular diastolic function [30] was significantly different in male and female cohorts along with end-diastolic left ventricular volume and end-diastolic left ventricular volume index, left ventricular stroke volume and left ventricular stroke volume index, left ventricular end-systolic long axis length and left ventricular end-systolic long axis length index, left ventricular end-diastolic free wall thickness and left ventricular end-diastolic free wall thickness index. Therefore, the ventricular diastolic function may be correlated with these parameters.

Although potential risk factors for sudden cardiac death for HCM in paediatric patients have been reported, there lack of standardised definitions for these risk factors [31]. In adults, major risk factor for HCM are well defined and reported in the guidelines. Factors such as family history of sudden cardiac death, maximum left ventricular wall thickness, abnormal blood pressure response during exercise are considered as major risk factors for sudden cardiac death whereas factors such as reduced ejection fraction or genetic mutations are considered as potential risk modifiers. [32,33]. Although this does not focus on the risk stratification for HCM in children, reported results may help to establish diagnostic criteria for the children around 14 years of age and affected by HCM.

There were a number of limitations in this study. There was no control group; however, the patients included in this study had been diagnosed with HCM. Therefore, the results give insights about cardiac dimensions in children around 14 years old and diagnosed with HCM. This study includes a relatively small sample size. Larger sample size would allow understanding differences between male and female patients better whilst providing a better estimate for the average values in children affected by HCM. Different phenotypes of HCM were not identified in the patient population. Therefore, the results do not show morphologic and functional changes for each type HCM. Also, this study includes patient characteristics from the initial diagnosis and magnetic resonance images. Therefore, the progress of the HCM is not reported in this study**.** Moreover, 3D models reconstructed from magnetic resonance image or stress echocardiography could bring new insights about the clinical characteristic of the pediatric patients with HCM during exercise. Also, myocardial fibrosis which may contribute to sudden cardiac death, ventricular tachyarrhythmias and ventricular dysfunction [34] was not evaluated in this study as it may not have an effect on the local contractile function [8].

In this study, ventricular dimensions, left ventricular wall thickness, and intraventricular septal thick-ness was quantified using cardiac magnetic resonance images in children diagnosed with HCM. Also, a statistical comparison was made to evaluate the differences between males and female patients. The results show that the left ventricular wall and intraventricular septal thickness increase affecting left ventricle cavity dimensions in children affected by HCM. There was statistically significant difference in the heart rate, end-diastolic left ventricular volume and end-diastolic left ventricular volume index, left ventricular stroke volume and left ventricular stroke volume index, left ventricular end-systolic long axis length and left ventricular end-systolic long axis length index, left ventricular end-diastolic free wall thickness and left ventricular end-diastolic free wall thickness index and EA ratio for male and female patients in the study population. Although the right ventricular end-diastolic long axis length and left ventricular end-diastolic mid-cavity diameter were statistically different in male and female patients, indexed values for these variables were not statistically different.

References

[1] Marian AJ, Braunwald E. Hypertrophic Cardiomyopathy: Genetics, Pathogenesis, Clinical Manifestations, Diagnosis, and Therapy. Circ Res 2017;121:749–70. https://doi.org/10.1161/CIRCRESAHA.117.311059.

[2] Canepa Marco, Fumagalli Carlo, Tini Giacomo, Vincent-Tompkins Justin, Day Sharlene M., Ashley Euan A., et al. Temporal Trend of Age at Diagnosis in Hypertrophic Cardiomyopathy. Circulation: Heart Failure 2020;13:e007230. https://doi.org/10.1161/CIRCHEARTFAILURE.120.007230.

[3] Pantazis A, Vischer AS, Perez-Tome MC, Castelletti S. Diagnosis and management of hypertrophic cardiomyopathy. Echo Res Pract 2015;2:R45-53. https://doi.org/10.1530/ERP-15-0007.

[4] Colan SD. Hypertrophic Cardiomyopathy in Childhood. Heart Fail Clin 2010;6:433–44. https://doi.org/10.1016/j.hfc.2010.05.004.

[5] Lipshultz Steven E., Law Yuk M., Asante-Korang Alfred, Austin Eric D., Dipchand Anne I., Everitt Melanie D., et al. Cardiomyopathy in Children: Classification and Diagnosis: A Scientific Statement From the American Heart Association. Circulation 2019;140:e9–68. https://doi.org/10.1161/CIR.0000000000000682.

[6] Shirani J, Pick R, Roberts WC, Maron BJ. Morphology and significance of the left ventricular collagen network in young patients with hypertrophic cardiomyopathy and sudden cardiac death. J Am Coll Cardiol 2000;35:36–44. https://doi.org/10.1016/s0735-1097(99)00492-1.

[7] Konno T, Chang S, Seidman JG, Seidman CE. Genetics of hypertrophic cardiomyopathy. Curr Opin Cardiol 2010;25:205–9. https://doi.org/10.1097/HCO.0b013e3283375698.

[8] Ismail TF, Hewins B, Jabbour A, Mistry N, Ferreira PF, Gulati A, et al. The relationship between interstitial fibrosis and contractile function in HCM: a combined T1-mapping and CSPAMM tagging study. Journal of Cardiovascular Magnetic Resonance 2012;14:O97. https://doi.org/10.1186/1532-429X-14-S1-O97.

[9] Chaowu Y, Shihua Z, Jian L, Li L, Wei F. Cardiovascular magnetic resonance characteristics in children with hypertrophic cardiomyopathy. Circ Heart Fail 2013;6:1013–20. https://doi.org/10.1161/CIRCHEARTFAILURE.113.000414.

[10] Prinz C, Farr M, Hering D, Horstkotte D, Faber L. The Diagnosis and Treatment of Hypertrophic Cardiomyopathy. Dtsch Arztebl Int 2011;108:209–15. https://doi.org/10.3238/arztebl.2011.0209.

[11] Arghami A, Dearani JA, Said SM, O'Leary PW, Schaff HV. Hypertrophic cardiomyopathy in children. Ann Cardiothorac Surg 2017;6:376–85. https://doi.org/10.21037/acs.2017.07.04.

[12] Schwammenthal Ehud, Nakatani Satoshi, He Shengqiu, Hopmeyer Joanne, Sagie Alex, Weyman Arthur E., et al. Mechanism of Mitral Regurgitation in Hypertrophic Cardiomyopathy. Circulation 1998;98:856–65. https://doi.org/10.1161/01.CIR.98.9.856.

[13] Authors/Task Force members, Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2733–79. https://doi.org/10.1093/eurheartj/ehu284.

[14] Kampmann C, Wiethoff CM, Wenzel A, Stolz G, Betancor M, Wippermann CF, et al. Normal values of M mode echocardiographic measurements of more than 2000 healthy infants and children in central Europe. Heart 2000;83:667–72. https://doi.org/10.1136/heart.83.6.667.

[15] Quarta G, Aquaro GD, Pedrotti P, Pontone G, Dellegrottaglie S, Iacovoni A, et al. Cardiovascular magnetic resonance imaging in hypertrophic cardiomyopathy: the importance of clinical context. Eur Heart J Cardiovasc Imaging 2018;19:601–10. https://doi.org/10.1093/ehjci/jex323.

[16] Ommen SR, Mital S, Burke MA, Day SM, Deswal A, Elliott P, et al. 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2020;142:e533–57. https://doi.org/10.1161/CIR.0000000000000938.
[17] Tunca Sahin G, Ozgur S, Kafali HC, Sevinc Sengul F, Haydin S, Guzeltas A, et al. Clinical characteristics of hypertrophic cardiomyopathy in children: An 8-year single center experience. Pediatrics International 2021;63:37–45. https://doi.org/10.1111/ped.14393.
[18] Wang S, Zhu C. Hypertrophic cardiomyopathy in children. Asian Cardiovasc Thorac Ann 2022;30:92–7. https://doi.org/10.1177/02184923211041285.
[19] Assaad IE, Gauvreau K, Rizwan R, Margossian R, Colan S, Chen MH. Value of Exercise Stress Echocardiography in Children with Hypertrophic Cardiomyopathy. Journal of the American Society of Echocardiography 2020;33:888-894.e2. https://doi.org/10.1016/j.echo.2020.01.020.
[20] Windram JD, Dragelescu A, Benson L, Forsey J, Shariat M, Yoo S-J, et al. Myocardial Dimensions in Children With Hypertrophic Cardiomyopathy: A Comparison Between Echocardiography and Cardiac Magnetic Resonance Imaging. Can J Cardiol 2016;32:1507–12. https://doi.org/10.1016/j.cjca.2016.06.014.
[21] Miller CA, Jordan P, Borg A, Argyle R, Clark D, Pearce K, et al. Quantification of left ventricular indices from SSFP cine imaging: impact of real-world variability in analysis methodology and utility of geometric modeling. J Magn Reson Imaging 2013;37:1213–22. https://doi.org/10.1002/jmri.23892.
[22] Nayak BK, Hazra A. How to choose the right statistical test? Indian J Ophthalmol 2011;59:85–6. https://doi.org/10.4103/0301-4738.77005.
[23] Kervancioglu P, Kervancioglu M, Tuncer MC, Hatipoglu ES. Left Ventricular Mass in Normal Children and its Correlation with Weight, Height and Body Surface Area. International Journal of Morphology 2011;29:982–7. https://doi.org/10.4067/S0717-95022011000300054.
[24] Marcomichelakis J, Withers R, Newman GB, O'Brien K, Emanuel R. The relation of age to the thickness of the interventricular septum, the posterior left ventricular wall and their ratio. International Journal of Cardiology 1983;4:405–15. https://doi.org/10.1016/0167-5273(83)90190-0.
[25] Majonga ED, Rehman AM, McHugh G, Mujuru HA, Nathoo K, Patel MS, et al. Echocardiographic reference ranges in older children and adolescents in sub-Saharan Africa. International Journal of Cardiology 2017;248:409–13. https://doi.org/10.1016/j.ijcard.2017.06.109.
[26] Regen DM, Graham TP, Wyse RKH, Deanfield J, Franklin RCG. Left-ventricular cavity dimensions in children with normal and dilated hearts. Pediatr Cardiol 1988;9:17–24. https://doi.org/10.1007/BF02279878.
[27] Chun EJ, Choi SI, Jin KN, Kwag HJ, Kim YJ, Choi BW, et al. Hypertrophic Cardiomyopathy: Assessment with MR Imaging and Multidetector CT. RadioGraphics 2010;30:1309–28. https://doi.org/10.1148/rg.305095074.
[28] Manganelli F, Betocchi S, Losi MA, Briguori C, Pace L, Ciampi Q, et al. Influence of left ventricular cavity size on clinical presentation in hypertrophic cardiomyopathy. American Journal of Cardiology 1999;83:547–52. https://doi.org/10.1016/S0002-9149(98)00911-4.
[29] Bozkurt S. Mathematical modeling of cardiac function to evaluate clinical cases in adults and children. PLOS ONE 2019;14:e0224663. https://doi.org/10.1371/journal.pone.0224663.
[30] Tissot C, Singh Y, Sekarski N. Echocardiographic Evaluation of Ventricular Function—For the Neonatologist and Pediatric Intensivist. Frontiers in Pediatrics 2018;6.
[31] Norrish G, Kaski JP. Risk stratification in childhood hypertrophic cardiomyopathy. Glob Cardiol Sci Pract n.d.;2018. https://doi.org/10.21542/gcsp.2018.24.

[32] Jordà P, García-Álvarez A. Hypertrophic cardiomyopathy: Sudden cardiac death risk stratification in adults. Glob Cardiol Sci Pract n.d.;2018. https://doi.org/10.21542/gcsp.2018.25.
[33] Steriotis AK, Sharma S. Risk Stratification in Hypertrophic Cardiomyopathy. Eur Cardiol 2015;10:31–6. https://doi.org/10.15420/ecr.2015.10.01.31.
[34] Ho CY, López B, Coelho-Filho OR, Lakdawala NK, Cirino AL, Jarolim P, et al. Myocardial Fibrosis as an Early Manifestation of Hypertrophic Cardiomyopathy. N Engl J Med 2010;363:552–63. https://doi.org/10.1056/NEJMoa1002659.

Figure Legends

Figure 1. Heart chamber and wall dimensions measured on the cardiac magnetic images. 1. left ventricular long axis length, 2. left ventricular mid-cavity diameter, 3. right ventricular long axis length, 4. right ventricular mid-cavity diameter, 5. intraventricular septal thickness, 6. left ventricular lateral septal diameter, 7. left ventricular free wall thickness, (LV and RV represent left and right ventricles).

Table Legends

Table 1. Average values and standard deviations of the patient data and haemodynamics, superscript *n* represents non-parametric statistical comparison, * shows the statistically significant differences between the groups. (LV represents left ventricle).

Table 2. Average values and standard deviations of the left and right ventricular dimensions, superscript *n* represents non-parametric statistical comparison, * shows the statistically significant differences between the groups. (LV, RV and IV represent left and right ventricle and intraventricular respectively)

Table 3. Reproducibility for the measurements. (ICC represents intra-class correlation coefficient, LV, RV and IV represent left and right ventricle and intraventricular respectively)