Characterization of Hypertrophic Cardiomyopathy Using Left Ventricular Regional Wall Thickness Derived from CMR Imaging

Soo-Kng Teo[1*], Xiaodan Zhao[2], Ru-San Tan[2,3], Liang Zhong[2,3], Yi Su[1]

[1]Institute of High Performance Computing, A*STAR, Singapore
[2]National Heart Centre, Singapore
[3]Duke-NUS Graduate Medical School, Singapore

Abstract

Hypertrophic cardiomyopathy (HCM) patients present unusual myocardial mechanics due to hypertrophied ventricular wall. The objective of this study was to assess the distribution of regional wall thickness for the left ventricle (LV) based on cardiac magnetic resonance (CMR) images in HCM patients compared against control subjects.

CMR scans were performed in 19 HCM patients and 9 healthy individuals. Border-delineated contours of the LV endocardial and epicardial surfaces throughout the entire cardiac cycle were used to reconstruct the 3D LV geometry for all participants using our in-house software (Cardiowerkz). The LV wall thickness is then computed for each individual vertex on the endocardial surface mesh using a ray tracing approach to the epicardial surface mesh (to obtain the perpendicular distance from the mesh vertex on the endocardial surface to the epicardial surface). The regional wall thickness is then characterized using the standard 16-segment American Heart Association (AHA) nomenclature by aggregating over all mesh vertices in the particular segment.

We observed the following results: (i) regional wall thickness for all 16 segments in HCM patients were significantly higher as compared to normal controls and (ii) distribution of regional wall thickness across 3 representative HCM subtypes appear visually different. The novelty of our approach is that it facilitates the visualization of the LV wall thickness distribution across the 16 AHA segments that potentially can be used to differentiate the various HCM subtypes.

1. Introduction

Hypertrophic cardiomyopathy (HCM) is one of the most common cause of sudden cardiac deaths and results from a relatively common genetic cardiac disorder. This genetic mutation affects approximately one individual out of every five hundred in the general population with an estimated annual mortality rate of 1-2% among the affected individuals [1,2]. This disorder causes a portion of the left ventricular (LV) myocardium to become thickened and enlarged (hypertrophy) eventually resulting in fibrosis. This abnormal hypertrophy of the myocardium leads to impairment of LV cardiac functions that in the worse scenario, results in sudden cardiac death without any prior warnings [1,3]. This is because HCM is asymptomatic, meaning that the affected individual exhibits no clear clinical symptoms. Clinical symptoms of impaired LV cardiac functions such as arrhythmias (abnormal heart rhythms), systolic and/or diastolic dysfunction, left ventricular outflow tract (LVOT) obstruction are possible manifestations of HCM but are not definitive for HCM diagnostics.

Clinical assessment of HCM is performed typically by measuring the LV wall thickness using echocardiography with a maximal thickness at the septum and free wall >= 15 mm used as the diagnostic criteria (In the presence of clinical predisposition, e.g. family history of HCM, LV wall thickness of 13 to 14 mm can be considered borderline) [4]. In addition, asymmetrical LV wall thickness (defined as the ratio of septal to free wall thickness) of between 1.3 and 1.5 is also considered to be abnormal. However, echocardiography may possibly be limited by the following: (i) poor quality of the acoustic window resulting in incomplete visualization of the LV wall, (ii) the lack of reproducibility of the acoustic windows for subsequent follow-ups and (iii) underestimation of wall thickness for the LV anterolateral wall. Furthermore, apical hypertrophy can potentially be missed without the use of contrast agent during echocardiography [5]. One of the main challenge in the diagnostic of HCM is also the differentiation between abnormal thickening of the LV myocardium in HCM individual versus exercise-induced thickening in "athlete's heart". This is because wall thickness for both groups are higher as compared to normal controls and additional clinical information (such as family history of HCM) are required for making a diagnostic.

The pattern of hypertrophy in affected individual is

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variable but can be broadly classified into the following subtypes: reverse curvature, sigmoid and neutral, apical HCM and mid-ventricular HCM. Appropriate identification of these morphological subtypes may be helpful for clinical management because the various patterns seem to be closely related to the presence (or absence) of a HCM-related genetic abnormality.

In this study, we proposed using LV regional wall thickness derived from cardiac magnetic resonance (CMR) imaging to characterize HCM patients. CMR, as compared to echocardiography, have the following advantages: (i) good spatial resolution due to the sharp contrast between the blood pool and LV myocardium and (ii) offers a complete tomographic imaging of the entire LV that is highly reproducible. This imaging modality thus provides clinicians an option to more accurately detect the presence as well as to measure the extend and distribution of LV hypertrophy in individual with HCM [6,7]. This regional wall thickness is computed from the reconstructed 3D geometry of the LV endocardial and epicardial surfaces derived from contouring of CMR images, and characterized using the standard 16-segment American Heart Association (AHA) nomenclature [8]. The advantage of our approach is that the LV wall thickness computed is reproducible and not subject to intra/inter-observer variabilities in measurement that are inherent in echocardiography. Furthermore, our approach also facilitates the visualization of the LV wall thickness across the 16 AHA segments that potentially can be used to differentiate the various HCM subtypes.

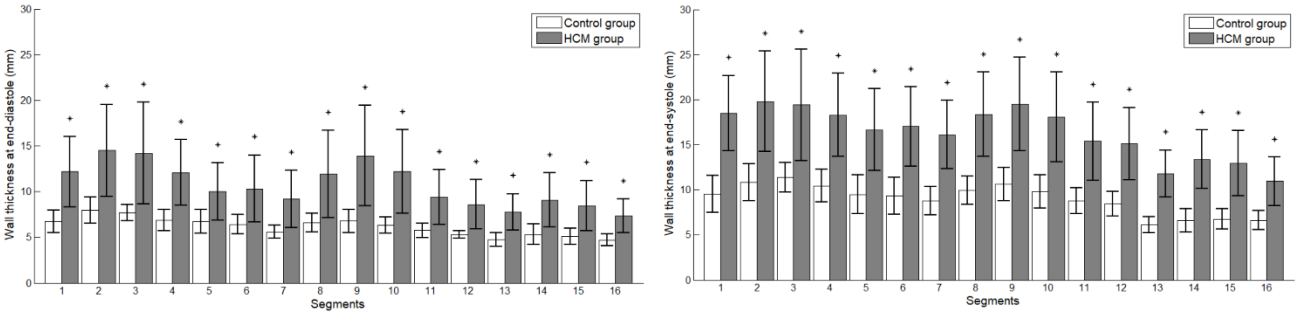

Figure 1. Comparison of the LV wall thickness (expressed as mean ± standard deviation) at ED (left) and ES (right) between the control group and HCM group. We observed that the regional wall thickness across all 16 segments in the HCM group were significantly higher compared to the controls group during both ED and ES (* $p < 0.05$). Refer to main text for further discussion.

2. Methods

2.1. Cine MRI

The proposed method was experimented on 19 HCM patients (male/female=11/8) and 9 age-matched normal control (male/female=8/1). The MR images were acquired on a 1.5T Siemens scanner with conventional ECG gating. The pixel spacing is 1.67 mm. The TR/TE/flip angle is typically 63.84/1:13/70º.

2.2. Reconstruction of 3D LV model

The method for the 3D geometrical model reconstruction of the LV is based on our approach published in previous work [9]. Firstly, the borders representing the endocardial and epicardial surfaces for the LV throughout the entire cardiac cycle are manually segmented from the short-axis CMR images by an experienced cardiologist. Secondly, these sets of segmented contours are used to reconstruct the endocardial and epicardial surface in the form of an unstructured triangle mesh using our in-house meshing code (Cardiowerkz). Next, a landmark reference point is defined by the cardiologist to indicate the anterior attachment junction of the right ventricular wall to the LV, to orientate the mesh to the corresponding anatomy. Finally, the reconstructed 3D mesh is partitioned into 16 segments to characterize the wall thickness distribution based on the American Heart Association nomenclature [8]. This partitioning is required to quantitate the regional wall thickness from the 3D geometrical model. In our approach, segment 17 is omitted because of the difficulty in acquiring the true apex position from the CMR images. The LV wall thickness is then computed for each individual vertex on the endocardial surface mesh using a ray tracing approach (to obtain the perpendicular distance from the mesh vertex on the endocardial surface to the epicardial surface). For mesh vertices on the most basal and apical slices, we noted that this ray tracing approach can potentially fail if the surface curvature at the vertex results in a projected ray that does not intercept the epicardial surface. For any such vertices, the wall thickness is not defined and excluded from subsequent calculation. The regional wall thickness is then characterized using the standard 16-segment AHA nomenclature by aggregating over all mesh vertices in the

particular segment. Further details of the mesh partitioning are published in Su et al., [9]. The robustness and reproducibility of this approach has also been demonstrated in our previous work [10].

at both ED and ES, with wall thickness decreasing from base to apex. In contrast, there were large variations in the wall thickness for the HCM group at both ED and ES, with the largest wall thickness appearing at the basal

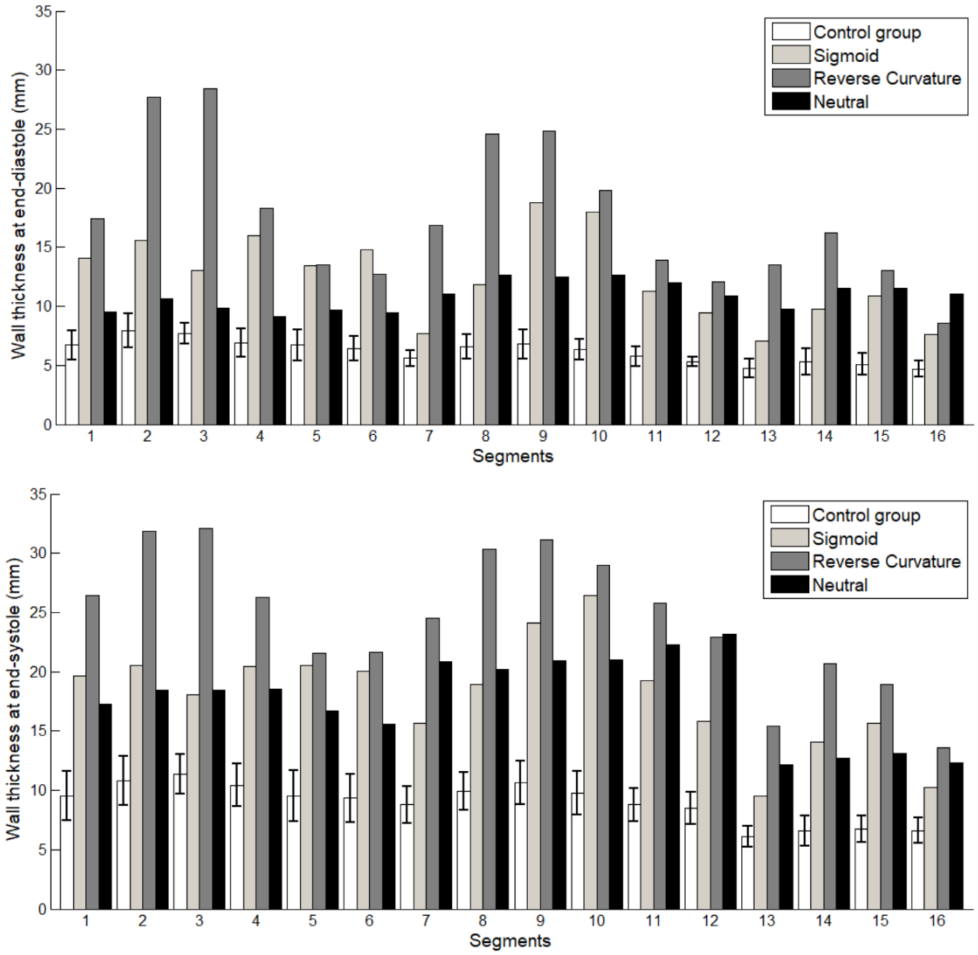

Figure 2. Distribution of LV wall thickness (expressed as mean ± standard deviation) across the 16 AHA segments for 3 representative HCM subtypes at ED (top) and ES (bottom) compared to the control group. We observed the following: (i) LV wall thickness in Reverse Curvature HCM is the most unevenly distributed with visible spikes in Segments 2, 3 (basal anterior and inferior septal respectively) and Segments 8, 9 (mid anterior and inferior septal respectively) as compared to the other 2 subtypes, (ii) LV wall thickness in Neutral HCM is the most evenly distributed with the smallest variations across segments, though still higher when compared to the control group and (iii) LV wall thickness in Sigmoid HCM appears to spike in Segments 9 (mid inferior septal) and 10 (mid inferior).

3. Results and Discussion

The LV wall thickness for all 16 segments at end-diastole (ED) and end-systole (ES) were computed for both HCM (n=19) and control (n=9) group (see Figure 1). We observed that the regional wall thickness in HCM patients were significantly higher as compared to normal controls at both ED and ES ($p < 0.05$ for all segments at both ED and ES). For the control group, wall thickness at basal (segments 1-6), mid-cavity (segments 7-12) and apical regions (segments 13-16) changed almost uniformly

anterior septal (Segment 2), basal inferior septal (Segment 3), mid anterior septal (Segment 8) and mid inferior septal (Segment 9). This observation is likely due to the presence of hypertrophied septum in HCM patients (see Figure 1). We also plotted the LV wall thickness for all 16 segments at ED and ES for 3 representative HCM subtypes: Sigmoid, Reverse Curvature and Neutral (see Figure 2) and its corresponding reconstructed 3D geometry (see Figure 3). We observed that each HCM subtypes has a distinct regional wall thickness distribution that correspond to the differing location of the hypertrophied myocardium in the respective subtypes. This difference in

the regional wall thickness distribution can be potentially to differentiate the various HCM subtypes.

4. Conclusion

We have developed a computational approach to calculate the regional wall thickness using the 16-segment AHA nomenclature by reconstructing the 3D LV geometries. From our study, we observed the following results: (i) regional wall thickness for all 16 segments in HCM patients were significantly higher compared to normal controls and (ii) distribution of regional LV wall thickness across 3 representative HCM subtypes appear visually different.

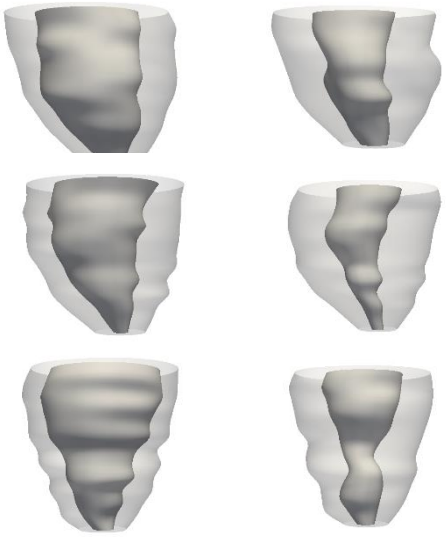

Figure 3. Reconstructed 3D LV geometry at ED (left) and ES (right) for three representative HCM subtypes: (top) Sigmoid, (middle) Reverse Curvature and (bottom) Neutral. Visually, we observed that there is a difference in the amount of abnormal wall thickening among these 3 subtypes, especially at ES.

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Address for correspondence.
Soo-Kng Teo.
1 Fusionopolis Way, #16-16 Connexis, Singapore 138632
teosk@ihpc.a-star.edu.sg