Classifying HCM Subtypes via Left Ventricular Two-Dimensional Curvature and Dynamic Time Wrapping

Min Wan, Yuli Yang, Xiaodan Zhao, Shuang Leng, Jun-Mei Zhang, Ru San Tan, Liang Zhong

Abstract

Identification of Hypertrophic cardiomyopathy (HCM) morphological subtypes has the same significance as diagnosis HCM due to the close relation of subtypes and genetic mutations. This study aims to automatically classify HCM cases into subtypes via two-dimensional endocardial curvature and dynamic time wrapping (DTW). A total of 19 HCM patients underwent cardiac magnetic resonance (CMR) scans. Endocardial boundaries were delineated on long axis images. Endocardial curvatures were computed. Dynamic time wrapping and its variant soft-DTW were used to quantify the dissimilarity between a pair of endocardial curvature series. The dissimilarity was utilized in classifiers. The classifier using DTW has a 0.84 in-sample accuracy and 0.58 out-of-sample accuracy. Soft-DTW has a 0.79 in-sample accuracy and 0.68 out-of-sample accuracy. We envision the use of this method in current clinical practice to improve the subtype identification efficiency and effectiveness.

1. Introduction

Being a primary disease of the cardiac sarcomere[1, 2], Hypertrophic cardiomyopathy (HCM) affects approximately one individual out of 500. The annual mortality rate is approximately 1-2%[3]. HCM is often characterized by the thickening and enlarged left ventricular (LV) myocardium[1, 3–5]. Asymptomatic HCM may progress to fibrosis and impairment of cardiac function, resulting in sudden cardiac death. Impaired LV cardiac function and left ventricular outflow tract (LVOT) obstruction are possible clinical symptoms of HCM. But assessment and diagnosis of HCM is typically performed by measuring LV wall thickness in echocardiography. The pattern of ventricular hypertrophy is highly variable and broadly categorized into the morphological subtypes: reverse curvature, sigmoid, and neutral [6].

Identification of the morphological subtype may have same significance of the diagnosis itself. Since morphological subtypes are related to genetic mutation. [6] showed that the majority (79%) of reverse curvature subtype were found to harbor a certain genetic mutation. While relatively a small percentage (16%) of other subtypes have such mutation. The frequency of various genetic mutations in all subtypes was reported in [6]. That meaningful results suggest subsequent genetic counseling and genetic testing after diagnosis of HCM. Manual identification of morphological subtypes could be performed via examining echocardiography.

Echocardiography has limitations in diagnosing HCM as well as identifying morphological subtypes. Due to the difficulty to visualize the hypertrophied myocardium part, echocardiography probably underestimate the extent of the LV wall thickening, especially for patients with the hypertrophied anterolateral wall [7]. Due to its high spatial resolution, intrinsic blood-to-tissue contrast and high reproducibility, cardiac magnetic resonance (CMR) has been considered the non-invasive gold standard for evaluating cardiac volume and ejection fraction, and deformation using feature tracking technique [8–11]. All above advantages make CMR a preferred imaging modality in identifying morphological subtypes [12]. Furthermore, three-dimensional geometric characteristics could be assessed more accurately, both regionally and globally [12–16]. In our previous studies [17, 18], we also report the regional wall thickness as a sensitive marker for diagnosis HCM and identification of subtypes.

However, all above indicators strongly depend on the establishment of the myocardium model, which demands delineation of both endocardium and epicardium. However, to delineate epicardium is not a trivial task. The boundary of epicardium is not obvious as that of endocardium. Manual delineation of epicardium requires experienced experts. Automatic epicardium delineation is still under experimental stage. Meanwhile, endocardium is easier to identify due to the high contrast between myocardium and blood pool. A lot of studies contribute to automatic endocardium segmentation. The demand to classify HCM subtypes using only endocardial characteristics motivates our study.

In this study, we proposed a method to classify HCM subtypes using only two-dimensional endocardial curves. Endocardial curves were delineated on three-chamber long axis images. Curvature on the endocardial curves were computed. The dissimilarity among curvature series of all cases was evaluated and utilized in subsequent classifiers. The remainder of this paper is organized as follows. Section 2 describes the methodology including (a) image
acquisition and processing; (b) curvature computation; (c) quantifying dissimilarity/discrepancy between two curvature series; (d) classifying HCM subtypes automatically.

Section 3 provides the experimental results and both qualitative and quantitative validation. The performance of algorithm is evaluated. Section 4 concludes this article.

2. Methods

The method proposed in this study consists of four stages: (1) Image acquisition and processing; (2) Curvature computation; (3) Quantifying similarity between curvature series; (4) Classifying subtypes based on similarity. The flowchart describing our method is shown in Figure 1. Alternative implementations are also included with illustration. Each stage will now be described in detail.

2.1. Study Population

The SingHealth Centralized Institutional Review Board approved this study for human research. All 19 patients were provided with comprehensive information about the study as well as the data collection and usage. The MR data are deposited in hospital and are available for research and educational purposes. Patients mean age was 51 ± 13 years, and 7 were male. All 19 cases were categorized by our senior HCM consultant as sigmoid (n = 6), reverse curvature (n = 8) or neutral (n = 5), according to the HCM subtype description in [6].

2.2. MR Scan and Processing

Cardiovascular magnetic resonance was performed in all patients on a 1.5T scanner (Avanto, Germany) using steady state, free precession (SSFP) cine gradient echo sequences. Parallel short axis images as well as radial long axis images (two-chamber, three-chamber, four-chamber) were acquired. Only three-chamber long axis image was used for analysis. The minimal requirement suggests that methods in this study could be adapted for echocardiography without much effort.

Left ventricular endocardial boundary were delineated by trained experts using CMRtools (Cardiovascular Solution, UK). The boundary curve was open at the atrioventricular annulus. Experts delineated the endocardial curve from posterior of mitral valvar orifice to anterior of aortic valvar orifice. An example of the delineated endocardial curve was shown in Figure 2. The middle of the curve was at left ventricular apex and the latter half of the curve was interventricular septum part. This guideline guaranteed the same direction for endocardial curves in all cases. Since the curve was in a counterclockwise direction, the obtained curvature shall be positive mostly.

2.3. Curvature Computation

Two-dimensional curvature of a planar curve could measure how sensitive or fast the tangent vector of the curve is rotating. The descriptive terms "convex" and "concave" frequently used in HCM myocardial morphology could be quantitized using curvature. Since the endocardial curves obtained were discrete curves consisting of discrete points, no analytic/parametric representation was available. The curvature could only be estimated using other points in some neighborhood instead of computed as in differential geometry. Discrete curvature estimation methods can be based on (1) derivative of the tangent angle; (2) radius of
the osculating circle; (3) derivative of the curve. We chose
the derivative of the curve implementation. For all 19 pa-
tients, we computed the endocardial curvature.

2.4. Quantifying Dissimilarity between Se-
ries

We can observe inter-subtype dissimilarity qualitatively.
To quantify the dissimilarity, we utilize dynamic time
wrapping (DTW) algorithm [19, 20]. Given two series
\( x = (x_1, \ldots, x_n) \in \mathbb{R}^n \) and \( y = (y_1, \ldots, y_m) \in \mathbb{R}^m \),
the cost matrix is defined as

\[
\Delta(x, y) := [\delta(x_i, y_j)]_{ij} \in \mathbb{R}^{n \times m} \tag{1}
\]

The inner product \( \langle A, \Delta(x, y) \rangle \) provides a score for the
alignment matrix \( A \). DTW is the least score among all
possible alignment matrices. Another alignment algorithm
Global Alignment kernel (GAK) [21] takes into account of
all alignment matrices.

\[
\text{DTW}(x, y) := \min_{A \in \mathcal{A}_{n,m}} \langle A, \Delta(x, y) \rangle \tag{2}
\]

Soft DTW [22] unifies the above two alignment and pro-
vides a smoothed dissimilarity measure.

\[
\text{min } \{a_1, \ldots, a_n\} := \begin{cases} 
\min_{1 \leq i \leq n} a_i, & \gamma = 0 \\
-\gamma \log \sum_{i=1}^{n} e^{-a_i/\gamma}, & \gamma > 0
\end{cases} \tag{3}
\]

\[
\gamma\text{-soft-DTW is defined as}
\]

\[
\text{dtw}_\gamma(x, y) := \min \{\langle A, \Delta(x, y) \rangle, A \in \mathcal{A}_{n,m}\} \tag{4}
\]

Two curvature series from two HCM cases were shown
in Figure 3 as well as their DTW alignment. The dissimi-
larity was used to classify the curvature series.

3. Results

Cine MR images were acquired for all 19 HCM pa-
tients and only three-chamber long axis ED frame was
processed. The average of manual delineation time using
CMRTools is about half minute. Curvature computation
average time is 5 ms on a 2.5 GHz CPU desktop. The
average time of DTW for one case is 0.7ms. Soft DTW
took about 0.15s for one case. Compared to the three-
dimensional geometric descriptors and shape reconstruc-
tion, two-dimensional curvature based methods are largely
efficient.

We used three types of dissimilarity measures in this s-
tudy, (1) Euclidean distance without alignment; (2) DTW
distance; (3) soft DTW distance.

All 19 cases were sub-categorized by a senior HCM
consultant. Classic K-nearest neighbors algorithm was also
trained to classify 19 cases into 3 subtypes. Classifi-
er performances were evaluated by both in-sample accu-
rracy and out-of-sample accuracy. Out-of-sample experi-
ments were conducted using leave-one-out (LOO) cross-
validation. The classifier accuracy for all three dissimilar-
ity measures were listed in Table 1. Euclidean distance
without alignment and DTW have a better in-sample ac-
ccuracy while soft-DTW has slightly better out-of-sample
accuracy. We believe soft-DTW has better generalization
capacity in future studies with more cases.

Table 1. Classifier performance based on different dissim-
ilarity measure

<table>
<thead>
<tr>
<th>Dissimilarity</th>
<th>In sample accuracy</th>
<th>LOO accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euclidean</td>
<td>0.79</td>
<td>0.52</td>
</tr>
<tr>
<td>DTW</td>
<td>0.84</td>
<td>0.58</td>
</tr>
<tr>
<td>Soft DTW</td>
<td>0.79</td>
<td>0.68</td>
</tr>
</tbody>
</table>

4. Discussion and Conclusion

In this study, we proposed a method to classify HCM
subtypes via two-dimensional endocardial curvature. A
pair of curvature series were aligned to each other to com-
pute their dissimilarity/discrepancy. Dynamic time wrap-
ing method and its variant soft-DTW were both used,
which could eliminate the effect of varying series lengths
and well capture the predominant characteristics in curva-
ture series. The dissimilarity (DTW distance) was used to
classify the curvature series into HCM subtypes. Classic
K-nearest neighbors methods were used. DTW and soft-
DTW obtain better classification accuracy than Euclidean
distance without alignment in our experiments.

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