Orthogonal Shape Modes Describing Clinical Indices of Remodeling

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Abstract. Quantification of the left ventricle (LV) shape changes (remodeling) is of great importance for therapeutic management of myocardial infarction. Orthogonal shape modes derived from principal component analysis (PCA) often do not describe clinical remodeling indices. We developed a method for deriving orthogonal shape modes directly from any set of clinical indices. Cardiac magnetic resonance images of 1,991 asymptomatic volunteers from the MESA study (age 44−84, mean age 62, 52 % women) and 300 patients with myocardial infarction from the DETERMINE study (age 31−86, mean age 63, 20 % women) were obtained from the Cardiac Atlas Project. Clinical indices of LV size, sphericity, wall thickness and apical conicity were calculated. For each index, cases outside two standard deviations of the mean, but within one standard deviation for all other indices, were chosen as a representative subgroup. Orthogonal modes were defined sequentially, using the first principal component of each subgroup. At each step, the contribution of the previous mode was removed mathematically from the shape description, similar to Gram–Schmidt orthogonalization. Correlation analysis and logistic regression were performed to show the effectiveness of these features to characterize remodeling due to myocardial infarction.

Keywords: Cardiac remodeling · Magnetic resonance imaging · Principal component analysis

1 Background

Left ventricular (LV) remodeling refers to the process by which ventricular size, shape and function are regulated by mechanical, neurohormonal and genetic responses to insult [1]. Myocardial infarction leads to LV remodeling of the heart, which provides important diagnostic information for the therapeutic management of ischemic heart disease [2–5].

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Remodeling associated with LV size is an important predictor of mortality after myocardial infarction [6], and changes of sphericalization of heart shape are linked with decreased survival [5]. LV wall thickness [1] and apical conicity [7] changes are also important indicators for LV infarction remodeling due to myocardial infarction.

Standard clinical indices used to describe remodeling are typically simple measures of mass and volume, such as end-diastolic (ED) volume (largest volume), end-systolic (ES) volume (smallest volume) or left ventricular mass. However, these ignore much of the available shape information. Principal component analysis (PCA) [8] is currently one of the most widely used feature extraction techniques. PCA projects the data onto a linear space of maximum-variation directions (known as modes) with orthogonal transformations. After the projection the first mode accounts for the maximum variance, and each succeeding mode in turn has the highest residual variance possible under the linear orthogonality constraint. PCA analysis of cardiac remodeling has been explored previously [9] showing that combined PCA modes can be more powerful descriptions of remodeling than traditional indices. Typically, the first PCA mode corresponds with LV size and the second typically with LV sphericity. Mode orthogonality is important for maintaining simplicity in many mathematical applications (e.g., flow computations [10]). However, PCA modes do not generally correspond well with clinically established indices of remodeling (e.g., wall thickness). We developed a novel methodology which captures the shape characteristics of a given clinical indicator while maintaining mode orthogonality. Clinically-defined indices of size, sphericity, wall thickness and conicity, known from the literature to be important in the management of myocardial infarction, were used to create a corresponding orthogonal linear space from the shape parameters.

Cardiac magnetic resonance images of 1,991 asymptomatic volunteers from the Multi-Ethnic Study of Atherosclerosis (MESA) [11] and 300 patients with myocardial infarction contributed from the Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation (DETERMINE) [12] study were obtained through the Cardiac Atlas Project [13] to create these novel clinically-defined modes. A logistic regression model on the MESA and DETERMINE data was established to explore the effectiveness of these modes to predict LV remodeling due to myocardial infarction.

2 Methods

Finite element models were customized to model the shape and function of each case using a standardized procedure [9]. For the MESA cohort, short-axis hand-drawn contours on the inner and outer surfaces of the left ventricle were available from the MESA MRI core laboratory. These contours were fitted by the finite element model by linear least squares as described previously [14, 15]. For the DETERMINE cohort, expert observers performed the analysis using guide-point modeling [16] to interactively customize a time-varying 3D cardiac finite element model of the LV to MR images using custom software (CIM version 6.0, University of Auckland, New Zealand). The shape models were evenly sampled at sufficient resolution to capture all visible features, which resulted in 2,738 Cartesian (x_i, y_i, z_i) points.

LV mass and volume at ED were subsequently calculated from the cardiac LV shape models. The sphericity index was calculated as the EDV divided by the volume of a sphere with a diameter corresponding to the major axis at end-diastole in LV long view [17]. The apical conicity index was calculated as the ratio of the apical axis (defined as the diameter of the endocardium one third above the apex) over the basal diameter [7]. Wall thickness was calculated as the mean distance between the corresponding endo- and epi-cardium surfaces.

For each clinical index, cases outside two standard deviations of the mean (95 % of variance). But within one standard deviation for all other indices, were chosen to form a patient subgroup linked with each clinical index. Orthogonal modes were defined sequentially, using the first principal component of each subgroup. At each step, the contribution of the previous mode was removed mathematically from the shape description, similar to the Gram–Schmidt orthogonalization algorithm [18], prior to the calculation of the principal component. Modes were defined in the following order: (1) LV size, (2) sphericity, (3) conicity, and (4) wall thickness.

Mathematically, let X^1 represent the shape space as a matrix where each column contains the coordinates of 3D points describing the shape of one case. Selecting cases with high and low EDV as previously described, a principal decomposition of this subgroup yielded a matrix of modes (M_k^1), so that

$$X_m^1 = \overline{X^1} + \sum_{k=1}^{K} \alpha_{mk}^1 M_k^1 \tag{1}$$

for each case m in the subgroup, where $\overline{X^1}$ represents the Euclidean mean, K is the total number of modes M_k^1, and α_{mk}^1 their corresponding projections (these are also referred to as weights or scores). The first mode (M_1^1) was used to describe the LV size variation. The projections of the first mode were then removed from the initial space for all cases, creating a new space X^2. A PCA of the resulting shapes for the subgroup consisting of high and low sphericity was then performed. The mode relating to sphericity was then defined to be the first principal component of this subgroup, i.e. M_1^2:

$$X_m^2 \overset{\text{def}}{=} X_m^1 - \alpha_{m1}^1 M_1^1 = \overline{X^2} + \sum_{k=1}^{K} \alpha_{mk}^2 M_k^2. \tag{2}$$

New mode M_1^2 was then subtracted from the shape space X^2, and the procedure repeated for the conicity (M_1^3) and wall thickness modes (M_1^4). Note that by construction M_1^{i+1} is orthogonal to M_1^i [18] and $\left\langle M_1^{1,2,3,4} \right\rangle$ generate an orthogonal linear sub-space of X^1.

3 Results

The orthogonal modes corresponding to size, sphericity, conicity and wall thickness are shown in Fig. 1. Linear correlation coefficients were calculated between the clinical

indices and the shape-mode scores ($\alpha_{.1}^{1,2,3,4}$) in the combined MESA and DETERMINE population. The linear correlation coefficient between the size score and EDV, sphericity score and LV sphericity index, wall thickness score and LV wall thickness, conicity sore and LV conicity index were 0.93, −0.87, 0.75 and −0.63 respectively (Table 1). The linear correlation coefficients among the clinical indices (Table 2), correlation coefficients among the mode scores (Table 3) and correlation coefficients between clinical indices and scores of the first four PCA modes of the original dataset (standard PCA in Table 4) were also calculated as a reference. It can be seen that, although the shape modes are orthogonal (their dot products are zero), some remodeling indices and corresponding mode scores were significantly correlated. In particular, the wall thickness score was significantly correlated with LV size, with larger hearts having thinner walls, consistent with eccentric remodelling. Also, although the first two standard principal components correspond with size and sphericity respectively, other components do not correspond with any particular remodeling index.

The clinically-derived shape modes described 39 %, 9 %, 6 % and 4 % of the total shape variation respectively, compared with 50 %, 10 %, 8 % and 7 % for the first four standard PCA modes. A logistic regression model was performed to evaluate the discriminatory power of the clinically-derived modes to characterize LV remodeling due to myocardial infarction. Age, sex, height, weight, systolic blood pressure (SBP), smoking status and diabetes status were used to establish a baseline model. The baseline model was established to give a control model consisting of common clinical factors known to be associated with myocardial infarction.

These variables were included in all the models since they may be confounding factors between the disease and shape features. The scores from the clinical modes show significant odds ratios in the myocardial infarction model (Table 5). The odds ratio of size, sphericity, wall thickness and conicity indicate that myocardial infarction patients tend to have larger and more spherical LV shapes with thicker walls, and a less conical shape. The area of receiver operating characteristic (ROC) curve (Fig. 2) for the clinical mode logistic classification model is 90.87 %, similar to the model using scores of the first four standard PCA modes (92.05 %).

Table 1. Correlation coefficients between the clinical indices and the clinical modes scores

	Size score	Sphericity score	Conicity score	Wall thickness score
EDV	0.93*	0.03	−0.03	−0.66*
Sphericity index	−0.06*	−0.87*	−0.05*	−0.04
Conicity index	−0.07*	0.29*	0.75*	0.08*
Wall thickness	0.37*	0.11*	−0.08*	−0.63*

Note: *indicates p value < 0.05 in all the tables of this paper

Table 2. Correlation coefficients between the clinical indices

	EDV	Sphericity index	Conicity index	Wall thickness
EDV	1.00	0.22*	−0.15*	0.14*
Sphericity index		1.00	−0.22*	−0.15*
Conicity index			1.00	−0.03
Wall thickness				1.00

Table 3. Correlation coefficients between the clinical mode scores

	Size score	Sphericity score	Conicity score	Wall thickness
Size score	1.00*	0.28*	0.001	−0.76*
Sphericity score		1.00	0.23*	−0.12*
Conicity score			1.00	0.09*
Wall thick score				1.00

Table 4. Correlation coefficients between the clinical indices and the first four modes of variation of X^1(standard PCA).

	EDV	Sphericity index	Conicity index	Wall thickness
PC1	−0.93*	0.06*	0.07*	−0.36*
PC2	−0.25*	−0.84*	0.39*	0.02
PC3	−0.05*	−0.18*	−0.25*	0.36*
PC4	0.06*	0.11*	−0.21*	−0.07*

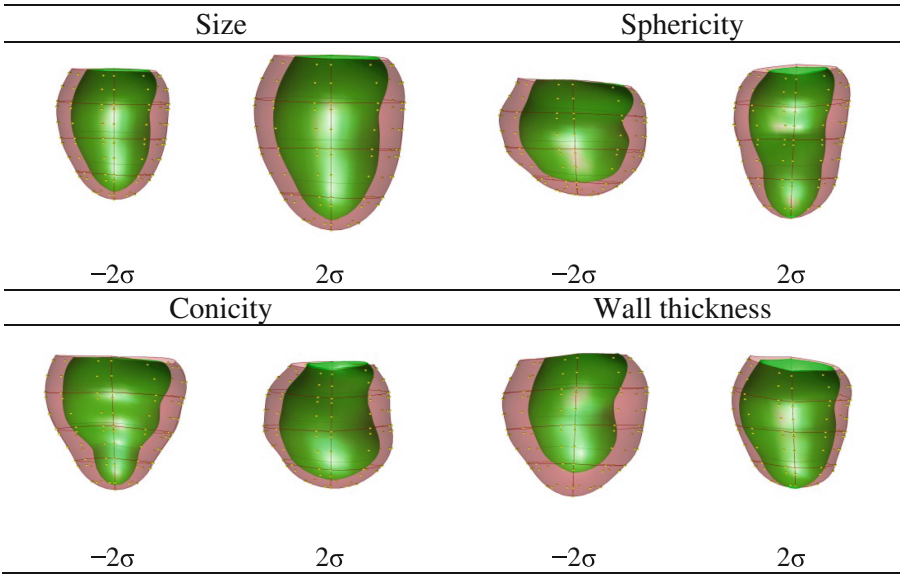

Fig. 1. Plot of the clinical modes

Table 5. Logistic regression analysis of the clinical modes to myocardial infarction

Parameter	Coefficient	Standardized coefficient	Odds ratio(OR)	OR 95 % Confidence interval	
Age*	0.041	0.231	1.042	1.023	1.060
Gender	−0.430	−0.118	0.651	0.394	1.075
Height*	0.031	0.178	1.032	1.007	1.057
Weight*	−0.041	−0.415	0.960	0.950	0.970
SBP*	−0.015	−0.173	0.985	0.977	0.994
Diabetes*	1.231	0.249	3.425	2.315	5.070
Smoke	−0.363	−0.066	0.696	0.420	1.153
Size*	0.020	1.408	1.020	1.018	1.023
Sphericity*	−0.009	−0.297	0.991	0.989	0.994
Conicity*	−0.008	−0.177	0.992	0.987	0.996
Wall thickness*	0.010	0.263	1.010	1.005	1.016

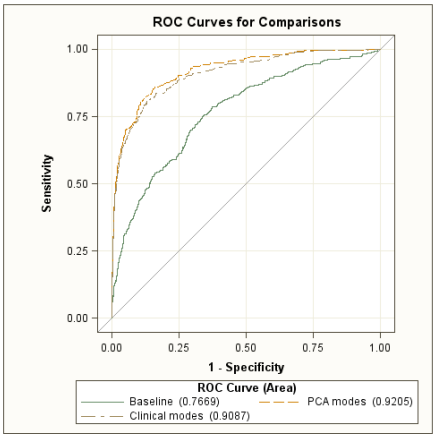

Fig. 2. ROC curve for the three logistic regression models

4 Discussion

Patients with myocardial infarction have significant shape differences with respect to the normal population, due to cardiac remodeling. An atlas-based analysis of cardiac remodeling has previously shown superior performance to traditional mass and volume analysis in large data sets [9]. The framework consists of three steps: (1) fitting a finite element model to the LV MR images, (2) feature extraction of the aligned shape parameters, and (3) quantification of the association between the features and disease using logistic regression. Although PCA provides orthogonal shape features, which describe the maximum amount of variation for the fewest number of modes, these modes typically do not correspond with clinical indices of cardiac remodeling. To avoid this problem, and maintain the advantage of orthogonal shape features, we developed a method to generate orthogonal shape modes from any set of clinical indices.

In this paper, we generated a linear shape sub-space from the finite-element parameters encoding the clinical indices of size, sphericity, wall thickness and conicity. These orthogonal modes derived from traditional remodeling indices may be used to partition shape variation in a similar way to PCA, but with a clinical rationale. Unlike PCA, correlation analysis shows that these clinically derived modes have high correspondence with traditional remodeling indices (Table 1). However, the absolute correlation decreases with increasing orthogonal modes, as the shape space is reduced by subtracting previous modes (Table 2). The clinical indices were moderately correlated (Table 2). Although the shape modes are orthogonal (zero dot product between different mode shape vectors) the mode scores are not guaranteed to be orthogonal in the statistical sense (uncorrelated), since size can be correlated with wall thickness in the human heart (Table 3). Furthermore, the proposed approach is dependent on the selection order of the clinical indices. Future work could look into the decorrelation of these scores by means of signal whitening, and also the difference of the shape modes obtained in different order.

In summary, we have demonstrated that clinically-derived modes quantitatively characterize remodeling features associated with myocardial infarction with similar accuracy to PCA modes. Compared with the baseline model, there was a significant incremental discriminatory power with the four clinical remodeling modes examined. This implies that these modes play an important role in cardiac remodeling. These clinical modes partition the variation into shape features which are linked to clinical outcomes and which have an intuitive visual interpretation.

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