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A Functional Data Analysis Approach to Left Ventricular Remodeling Assessment

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***Abstract*— Left ventricular remodeling is a mechanism common to various cardiovascular diseases affecting myocardial morphology. It can be often overlooked in clinical practice since the parameters routinely employed in the diagnostic process (e.g., the ejection fraction) mainly focus on evaluating volumetric aspects. Nevertheless, the integration of a quantitative assessment of structural modifications can be pivotal in the early individuation of this pathology. In this work, we propose an approach based on functional data analysis to evaluate myocardial contractility. A functional representation of ventricular shape is introduced, and functional principal component analysis and depth measures are used to discriminate healthy subjects from those affected by left ventricular hypertrophy. Our approach enables the integration of higher informative content compared to the traditional clinical parameters, allowing for a synthetic representation of morphological changes in the myocardium, which could be further explored and considered for future clinical practice implementation.**

***Index Terms*— ventricular remodeling, functional data analysis, computational anatomy, cardiac imaging**

I. Introduction

Left Ventricular (LV) remodeling is a mechanism involving significant morphological alterations of the ventricle. Such alterations typically include the increase of the myocardial mass and the alteration of the ratio between ventricular wall and chamber volume. This phenomenon leads to a deformation of the shape of the inner ventricular wall. These modifications often are a consequence of conditions as hypertension and obesity [1]. Since these modifications can alter the pump function, LV remodeling is a crucial factor in cardiac diseases [2]. The indicator of pump functionality most often employed in clinical practice is the Ejection Fraction (EF), defined as:

$$EF = \frac{EDV - ESV}{EDV}$$

Recent literature has often challenged the adequacy of EF as a marker of LV remodeling claiming that it can overlook significant morphological modifications, thus failing in assessing structural and functional changes in the myocardium [3]. These limitations are especially evident when this parameter is employed to evaluate myocardium contractility [4]. The modifications in the myocardium leading to a decreased end-diastolic volume (EDV) may also affect the end-systolic volume (ESV), resulting in an apparently physiological proportion between the two, actually underlying a pathological remodeling of both atria and ventricles [5]. The imaging techniques used in the diagnosis of LV remodeling are cardiac magnetic resonance and echocardiography. However, their evaluation remains mainly of a qualitative and subjective nature. Thus, quantitative indicators related to the LV morphology would be helpful in the clinical practise.

From such a context, it stems the necessity to develop new approaches to synthesize the data derived from cardiac imaging techniques. Computational anatomy has emerged as a new field integrating clinical knowledge in a mathematical framework to accurately assess anatomical structures by describing them through sets of volumes, curves, landmarks, and tensors [6]. Functional Data Analysis (FDA) offers a class of statistical methods developed to analyze curves that can be employed to extract and analyze anatomical features otherwise not observable.

In the present work, we propose an FDA approach to evaluate morphological modifications of the left ventricular walls (i.e. LV remodelling) by means of the inner contours acquired through cardiac magnetic resonance scans. We believe a similar approach could highlight some aspects undetectable using the methods currently employed in clinical practice. We validate this approach on patients affected by left ventricular hypertrophy, a pathology which does not affect clinical parameters as EF, EDV or ESV. We analyzed the cardiac magnetic resonance scans of 21 subjects, 12 of which affected by left ventricular hypertrophy and 9 healthy, whose ventricular inner and outer contours had been manually segmented by practitioners, both at the end-diastolic and end-systolic instants. For each subject, we develop a mathematical representation of the diastolic and systolic ventricular walls alongside a curve mimicking the EF definition to represent the cardiac muscle contractility. We reduce the dimensionality of these functional data through Functional Principal Component Analysis (fPCA) [7] and functional Depth Measures [8]. We employ a Quadratic Discriminant Analysis (QDA) to discriminate between hypertrophic and

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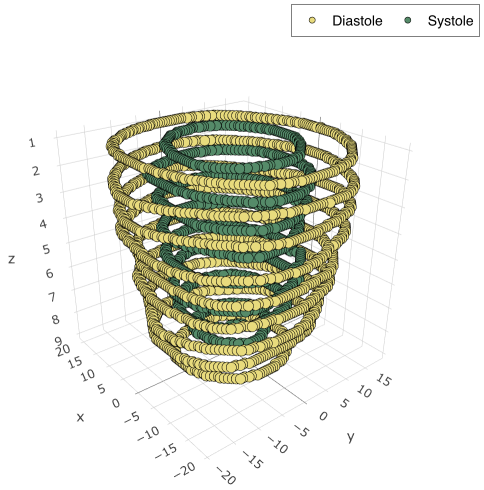

Fig. 1: XYZ coordinates of the inner left ventricle contours as segmented in a cardiac magnetic resonance scan at the end-diastolic (yellow) and end-systolic (green) instants. The base of the heart corresponds to the top of the figure. The example here displayed is relative to a healthy subject.

healthy subjects to evaluate the adequacy of functional parameters and compare them to the clinical ones.

II. Methods

In this section, we describe the dataset used and the analysis carried out in the present work. Our approach consists of three main steps: the representation of ventricle contours as curves, dimensionality reduction, and the evaluation of their ability to discriminate between healthy and hypertrophic subjects.

A. Data

The cardiac magnetic resonance scans treated in the present work are collected and made available online by the Sunnybrook Health Science Center, Toronto, Canada [9]. The dataset includes 21 patients (12 affected by left ventricular hypertrophy and 9 healthy), aged 57.67 $\pm$ 14.20 years and 60.67 $\pm$ 18.30 years, respectively.
For each subject the dataset provides 20 frames in 6–12 short-axis slices obtained scanning the heart from the base to apex. Image parameters are: thickness = 8 mm, image size = 256 × 256 pixels, FOV = 320 mm × 320 mm. In the present analysis we considered the images acquired at end-diastolic and end-systolic instants. In all the images, inner ventricular contours were manually segmented by practitioners and made available as Cartesian coordinates. The data used in the present work consisted of this manual segmentation. As an illustrative example, in Fig. 1 we display the data of a healthy subject.

B. Ventricular contours representation

To emphasize the morphological information contained in ventricular contours, we represent them as curves. First, we center each slice contour in their barycenter by converting the pixel coordinates from Cartesian to polar ones. We assign a progressive index to each pixel of a subject *i* starting from the top-left of the slice closer to the heart base and progressing along its contour. Once the slice is spanned, we move to the next slice's top-left point toward the apex. We will refer to the version of this index normalized by the number of pixels per subject as *abscissa*.
Finally, we obtain the curve representing the ventricle profile by computing the Euclidean distance of a pixel from the slice's center for each abscissa's value. These curves can be considered as functions of the abscissa and they can thus be assessed through Functional Data Analysis (FDA) tools. In conclusion, for each subject we define:

- a function computed at end-diastolic instant (*functional Diastole (fD)*);
- a function computed at end-systolic instant (*functional Systole (fS)*);
- a normalized difference of the previous two functions: $fEF = \frac{fD - fS}{fD}$ (*functional Ejection Fraction (fEF)*).

C. Dimensionality reduction

To remove noise, we firstly interpolate each curve with cubic B-splines [10]. This representation enabled us to compute the functions' first derivatives (*fD'*, *fS'*, *fEF'*). Since our interest lies in the ventricle's wall's curvature, we consider the latter for the analysis rather than the functions themselves. Moreover, to avoid redundancy, we focus the analyses on *fS'* and *fEF'* only.
In order to extract informative content from the data we apply two different FDA techniques of dimensionality reduction: fPCA and functional Depth Measures. The first is an extension of the well-known Principal Component Analysis (PCA) to functional data. We perform fPCA on *fS'* and *fEF'* independently in order to extract the most important features [10], [11].
Secondly, we compute Depth Measures for functional data, a class of robust statistics that assesses the centrality of a curve respect to a population of functions. The functional relative Modified Bandwidth Depth (rMBD) measure is obtained for all subjects with respect to one of the groups, as previously described in the literature [8]. Without loss of generality, we consider the hypertrophic group as the reference.

D. Discrimination between healthy and hypertrophic patients

The indexes obtained (fPCA scores and rMBD) are then compared with volumetric parameters (EF and ESV) in terms of informative content by means of QDA. Finally, we consider as performance indicators the Area Under the Curve (AUC) and the accuracy of the QDA given in input either traditional clinical parameters, fPCA scores or rMBD. To correctly estimate the performance that this model could reach on new data, we apply the procedure based on bootstrap proposed by Efron in [12]. Indeed, non-parametric bootstrap can be used for model validation since it allows to estimate the bias of a statistic (i.e., accuracy and AUC) which can be considered a measure of how overfitted the

statistics are. The indicators adjusted for the overfitting can be obtained by subtracting the estimated bias from the original dataset's performance metrics.

III. Results

In this section, we present the data representation obtained through the pre-processing previously explained, the output of the functional dimensionality reduction methods, and the performance obtained when using them to discriminate between groups of subjects.

A. Clinical Parameters

The substantial overlap of the hypertrophic and healthy subjects for what concerns clinical parameters is made evident by Fig. 2: the distributions of ESV and EF are very similar between the two groups (Wilkoxon Sum-Rank Test: p=0.46 for ESV and p=0.55 for EF). Moreover, the majority of patients regardless exceeds the 50% threshold in EF over which the parameter is considered in the physiological range.

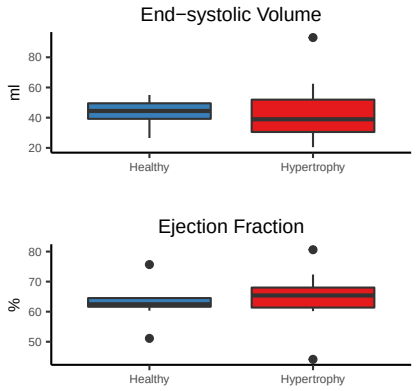

Fig. 2: Boxplots representing the distribution of the end-systolic volume (top panel) and ejection fraction (bottom panel) in healthy (blue) and hyperthrophic (red) subjects

B. Ventricular contours representation

As an example, Fig. 3 depicts two subjects' functional representation. We can observe a downward trend in the top panel (for diastole) due to the ventricle shape. The curve's beginning corresponds to the basis of the ventricle, whose diameter narrows as we move to the apex. On the other hand, the fluctuation of the curves is due to the ventricle walls' irregularity. Moreover, this peculiarity is highlighted in the functions' first derivatives (Fig. 4) and it appears to be enhanced in the subjects affected by hypertrophy.

C. Dimensionality reduction

In fPCA, the proportion of variance explained for *fS'* reaches 58% with the fifth PC. Afterwards the increment per each PC is small and, therefore, in the following analysis the scores up to the fifth principal component are considered. On the contrary, the *fEF'* second PC succeeds in explaining the entire variance content of the curve.

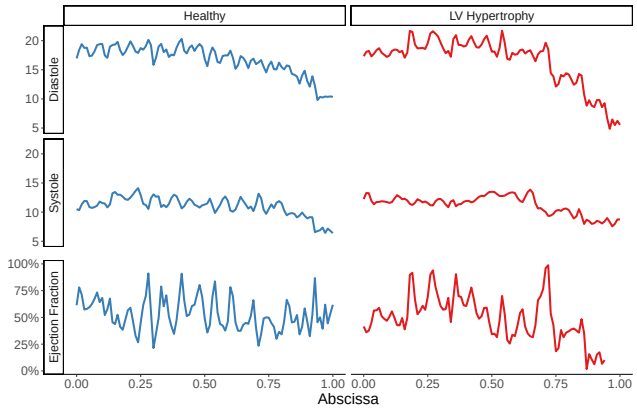

Fig. 3: Curves representing the inner left ventricle contours with respect to the abscissa. Left: curves of one healthy subject at end-diastolic instant (top panel), end-systolic instant (middle panel), and ejection fraction (bottom). Right: curves of one hypertrophic subject during end-diastolic instant (top panel), end-systolic instant (middle panel) and ejection fraction (bottom).

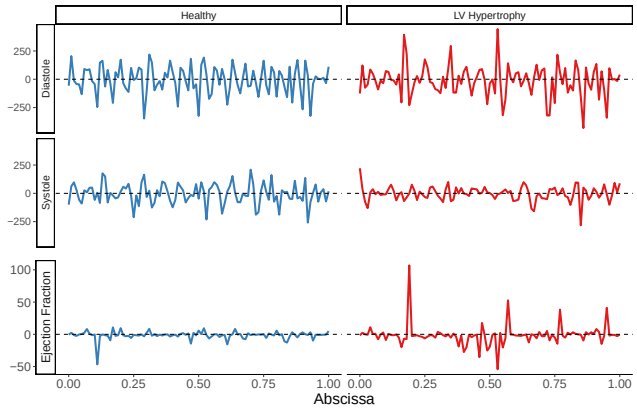

Fig. 4: First derivatives of the inner left ventricle contours with respect to the abscissa. Left: curves of one healthy subject at end-diastolic instant (top panel), end-systolic instant (middle panel) and ejection fraction (bottom). Right: curves of one hypertrophic subject during end-diastolic instant (top panel), end-systolic instant (middle panel) and ejection fraction (bottom).

The rMBD distributions in the two populations are compared through the boxplots in Fig. 5. For both for *fS'* and *fEF'* they are well separated between the two groups (Wilkoxon Sum-Rank Test: p=0.02 for both groups).

D. Discrimination between healthy and hypertrophic patients

It's clear that the functional approaches hereby proposed outperform the clinical parameters, both in terms of accuracy and AUC (Table I), even if the performance of the QDA models may still be optimistic, albeit corrected through the

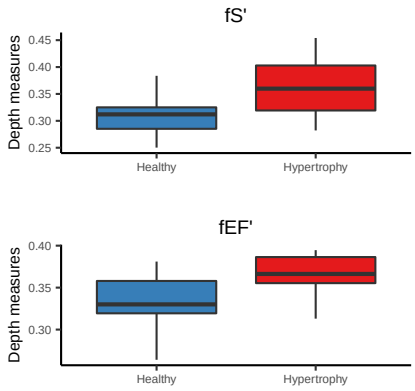

Fig. 5: Top panel: boxplots of relative Modified Bandwidth Depth of *fS'* separated per subject group; bottom panel: boxplots of relative Modified Bandwidth Depth of *fEF'* separated per subject group;

bootstrap method described in the previous section. The two functional measures reach satisfying performances: while the model with fPCA score has the highest accuracy (98.2%), the one with rMBD scores is the best in terms of AUC (92.8%).

TABLE I: Performance of Discriminant Analysis

	Accuracy (%)	**AUC (%)**
Clinical Parameters	65.96	59.15
fPCA Scores	98.20	83.96
Depth measures	85.59	92.79

The fact that the functions' first derivatives successfully discriminate the two subpopulations highlights how the most important differences between the two groups lie in the slope of the ventricular wall. More specifically, the discriminating features may be interpreted as the irregularity of the ventricular contours, more evident in hypertrophic subjects.

IV. Discussion & Conclusions

In this work we propose a new approach for the assessment of left ventricular remodeling by means of Functional Data Analysis. The novelty of this approach consists in the quantitative assessment of morphological information regarding the whole ventricle exploiting a functional data representation.
To evaluate the potentiality of the presented approach, we tackle the left ventricular hypertrophy, as this pathology is known to importantly affect the myocardial shape, while leaving unaffected its volume. We take into special account the first derivatives of all the curves to capture changes in the shape of the cardiac muscle. Functional Principal Component Analysis and Depth Measures are employed for dimensionality reduction and they both show interesting results. From our results, it is evident that this approach allows to obtain an informative summary of the left ventricular morphology and functionality. Indeed, with the method hereby proposed we manage to obtain a discrimination accuracy of 98%, while the traditional metrics only reach the 65%. Therefore, this line of research could lead to the identification of new parameters to be introduced in clinical practice to spot earlier modifications in the cardiac morphology.
In the future, we plan to extend the analysis described in this pilot study to a wider pool of subjects and to include different pathologies involved in left ventricular remodeling. Moreover, we aim to investigate its performance when given in input automatically segmented contours, in order to integrate it with novel medical imaging software. Finally, the proposed approach could be explored and applied to the risk stratification of patients affected by different cardiovascular diseases.

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