Image-based left ventricular shape analysis for sudden cardiac death risk stratification

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BACKGROUND Low left ventricular ejection fraction (LVEF), the main criterion used in the current clinical practice to stratify sudden cardiac death (SCD) risk, has low sensitivity and specificity.

OBJECTIVE To uncover indices of left ventricular (LV) shape that differ between patients with a high risk of SCD and those with a low risk.

METHODS By using clinical cardiac magnetic resonance imaging and computational anatomy tools, a novel computational framework to compare 3-dimensional LV endocardial surface curvedness, wall thickness, and relative wall thickness between patient groups was implemented. The framework was applied to cardiac magnetic resonance data of 61 patients with ischemic cardiomyopathy who were selected for prophylactic implantable cardioverter-defibrillator treatment on the basis of reduced LVEF. The patients were classified by outcome: group 0 had no events; group 1, arrhythmic events; and group 2, heart failure events. Segmental differences in LV shape were assessed.

RESULTS Global LV volumes and mass were similar among groups. Compared with patients with no events, patients in groups 1 and 2 had lower mean shape metrics in all coronary artery regions, with statistical significance in 9 comparisons, reflecting wall thinning and stretching/flattening.

CONCLUSION In patients with ischemic cardiomyopathy and low LVEF, there exist quantifiable differences in 3-dimensional endocardial surface curvedness, LV wall thickness, and LV relative wall thickness between those with no clinical events and those with arrhythmic or heart failure outcomes, reflecting adverse LV remodeling. This retrospective study is a proof of concept to demonstrate that regional LV remodeling indices have the potential to improve the personalized risk assessment for SCD.

KEYWORDS Sudden cardiac death; Cardiac magnetic resonance imaging; Computational anatomy; Shape analysis; Risk stratification; Implantable cardioverter-defibrillator

ABBREVIATIONS **2D** = 2-dimensional; **3D** = 3-dimensional; **AHA** = American Heart Association; **CMR** = cardiac magnetic resonance; **HF** = heart failure; **ICD** = implantable cardioverter-defibrillator; **LAD** = left anterior descending; **LV** = left ventricular; **LVEF** = left ventricular ejection fraction; **RWT** = relative wall thickness; **SAD** = sudden arrhythmic death; **SCD** = sudden cardiac death; **TEI** = transmural extent of the infarct; **WT** = wall thickness

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Introduction

Sudden cardiac death (SCD) is a major health problem worldwide, affecting hundreds of thousands of persons annually in the United States alone.[1] As the survival rate of SCD is very small, it is of paramount importance to identify patients at risk and give them prophylactic treatment. It is also crucial that the patient identification method is specific, as implantable cardioverter-defibrillator (ICD) therapy, the most widespread preventive care for SCD, is costly and associated with serious risks.[1] However, the patient selection criterion used in the current clinical practice, namely, left ventricular ejection fraction (LVEF) ≤35%, has low sensitivity and specificity.[2] Although numerous alternatives to SCD risk stratification have been proposed, the optimal approach remains unknown.[3]

It has been known for decades that cardiomyopathies are associated with adverse remodeling of left ventricular (LV) geometry, including LV dilation, wall thinning, and shape alterations and that this remodeling predicts overall morbidity and cardiovascular mortality.[4] Patient-specific LV geometry can now be analyzed with unprecedented accuracy, with recent advances in image-based data acquisition and analysis. On one hand, clinical cardiac magnetic resonance (CMR) imaging and its combination with late gadolinium enhancement can effectively and noninvasively acquire global indices of 3-dimensional (3D) LV structure in health and disease.[1] On the other hand, the new field of computational anatomy offers rigorous mathematical and algorithmic tools

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for the detailed assessment of segmental differences in image-based cardiac geometry.[5] Leveraging these advances to incorporate regional metrics of LV remodeling may help identify patients at a higher vs lower risk of SCD. Ideally, an anatomical biomarker could also differentiate patients with a high risk of SCD from those who do not have SCD outcomes but instead eventually succumb to heart failure (HF), which is an important competing cause of death in patients with cardiomyopathy and for which the management approach can be quite different.

The overarching goal of our research is to uncover novel, image-based, 3D indices of LV geometry that can be used to predict SCD risk specifically. The present study is a proof of concept, in which we have implemented a framework that uses CMR, advanced image processing, and computational anatomy tools to compare 3D LV endocardial surface curvature, wall thickness (WT), and relative wall thickness (RWT) between patient groups. We have retrospectively applied our methodology to data from patients with ischemic cardiomyopathy who were selected for ICD implantation on the basis of reduced LVEF, followed by implantation for clinical events, and divided into groups with differing SCD risk on the basis of follow-up time. We hypothesized that 3D LV shape metrics could identify patients at the highest risk for SCD. We also explored whether shape metrics alone could differentiate between SCD and HF outcomes.

Methods

Our framework is outlined in Figure 1, which shows how a patient heart image is processed with our pipeline, including reconstruction of 3D LV geometry, segmentation of endocardial surface, computation of 3D shape metrics, and regionwise statistical analysis. The data acquisition and the components of the pipeline are described in the following sections.

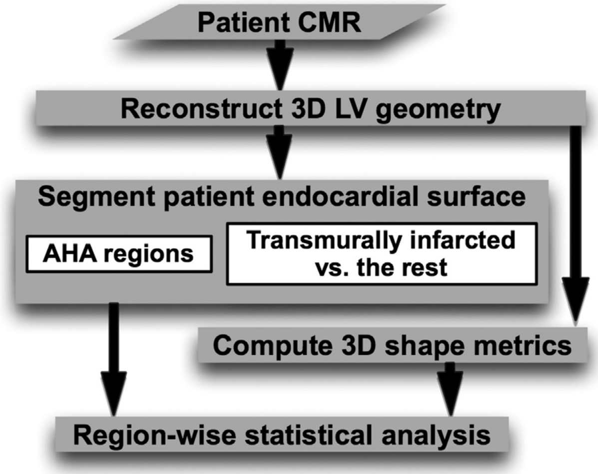

Figure 1 The processing pipeline of our computational framework. 3D = 3-dimensional; AHA = American Heart Association; CMR = cardiac magnetic resonance; LV = left ventricular.

Data acquisition

The data used for the present study consisted of late gadolinium–enhanced cardiac magnetic resonance images of 61 patients with ischemic cardiomyopathy and LVEF $\leq$35%, which represented a random sample from the CMR arm of the prospective observational study of implantable cardioverter-defibrillators at Johns Hopkins University.[1] In the CMR arm of the prospective observational study of implantable cardioverter-defibrillators, all patients were imaged, implanted with ICDs for the primary prevention of SCD, and then followed for events, including appropriate ICD firings, sudden arrhythmic death (SAD), and death or hospitalization due to HF. We divided the 61 patients into 3 groups: group 0 consisted of 28 patients with no events during follow-up, group 1 included 18 patients who either suffered from SAD or whose ICDs fired appropriately, and group 2 composed of 15 patients who died of or were hospitalized for HF, but did not have an arrhythmic event. Patients who had both an arrhythmic event and HF were included in group 1 (for more details, see Section 1 in the Online Supplement).

Reconstruction of 3D LV geometry

In each short-axis slice of the image, the LV endocardium and epicardium were semiautomatically contoured. The septal part of the endocardial contour was then manually identified by placing 2 landmark points near the right ventricular insertion points (Figure 2A). Investigators who performed the contouring and landmark placement were blinded to the patient groups. From the contours and landmark points, 3 sets of 2-dimensional (2D) binary masks, each set implicitly representing the LV endocardium, LV epicardium, and septal endocardium were constructed (Figure 2B). Each set of 2D masks was then interpolated to build a 3D binary mask at 1 mm isotropic resolution.[6] Finally, the geometry image of the LV wall was generated by combining the three 3D masks (Figure 2C) (for more details, see Section 2 in the Online Supplement).

Computation of shape metrics

For each image voxel along the endocardial surface, curvedness of the surface as well as WT and RWT of the LV were computed. Curvedness characterizes the deviation of a surface from flatness and is defined as the root mean square of principal curvatures.[7] We computed the principal curvatures as described in Goldman[8] from a Gaussian-smoothed version of the 3D mask for the LV chamber illustrated in Figure 2C. The WT at an endocardial surface voxel was calculated as the distance to the nearest voxel that lied along the epicardium. The RWT at an endocardial surface voxel was computed as the product of curvedness and WT at that voxel (Figure 3). This definition of RWT is our 3D extension of a 2D echocardiographic concept,[9] where RWT is defined as the ratio of posterior or septal WT to radius of the LV endocardium in diastole. Since curvedness is the inverse of radius,[7] the product of curvedness and WT is a measure of RWT (for more details, see Section 3 in the Online Supplement).