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Semi-automated Image Segmentation of the Midsystolic Left Ventricular Mitral Valve Complex in Ischemic Mitral Regurgitation

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Abstract

Ischemic mitral regurgitation (IMR) is primarily a left ventricular disease in which the mitral valve is dysfunctional due to ventricular remodeling after myocardial infarction. Current automated methods have focused on analyzing the mitral valve and left ventricle independently. While these methods have allowed for valuable insights into mechanisms of IMR, they do not fully integrate pathological features of the left ventricle and mitral valve. Thus, there is an unmet need to develop an automated segmentation algorithm for the left ventricular mitral valve complex, in order to allow for a more comprehensive study of this disease. The objective of this study is to generate and evaluate segmentations of the left ventricular mitral valve complex in pre-operative 3D transesophageal echocardiography using multi-atlas label fusion. These patient-specific segmentations could enable future statistical shape analysis for clinical outcome prediction and surgical risk stratification. In this study, we demonstrate a preliminary segmentation pipeline that achieves an average Dice coefficient of 0.78 ± 0.06 .

Keywords

Multi-atlas label fusion; Ischemic mitral regurgitation; 3D echocardiography

1 Introduction

Ischemic mitral regurgitation (IMR) is a disease in which the mitral valve is dysfunctional due to left ventricular remodeling after a myocardial infarction. The two most common surgical treatments of severe IMR are mitral valve repair with annuloplasty and mitral valve replacement. The trade-off between these treatments presents a surgical dilemma. Mitral valve repair avoids risks related to mechanical and prosthetic valve replacement and, in the largest and first randomized control trial, has been shown to produce the best outcomes when patients do not experience disease recurrence post-repair [1,2]. However, the same trial demonstrated that approximately 60% of patients undergoing mitral valve repair experience disease recurrence within 24 months [1,2]. Thus, there is an urgent need to understand and predict post-repair IMR recurrence in the immediate pre-operative setting. The problem of post-surgical recurrence can be significantly reduced if repair is only applied to patients in which durable repair is likely.

Recent studies have attempted to solve this problem by extracting and quantifying mitral valve features, such as leaflet tethering angles, from pre-operative 3D transesophageal echocardiography (TEE) for prediction of IMR in the early post-operative period [4]. While these features show great promise in predicting post-surgical disease recurrence, the most predictive features, thus far, have been ventricular features, such as the presence of a basal aneurysm [3,9]. This is expected as the etiology of IMR is primarily ventricular, and mitral valve dysfunction is secondary to geometric ventricular distortions. To our knowledge, the study of ventricular wall and shape parameters has either been primarily qualitative or has involved laborious manual measurements [3]. As a next step, it is imperative to study the integrated left ventricular mitral valve (LVMV) complex in a consistent and reproducible manner rather than to study the anatomical structures in isolation. It is equally important to automate the segmentation of TEE images in order for LVMV analysis to integrate into the operating room work flow. Previous studies have regionally segmented the left ventricle in isolation with a variety of methods, such as deep learning [13] and active surfaces [14], from different modalities, such as 3D computed tomography (CT) [6] and magnetic resonance imaging (MRI) [7,12], with excellent results. The majority of this research has not been focused on the IMR patient population or pre-operative TEE imaging and has been targeted towards making rapid measurements of left ventricular volume [14]. While these efforts represent the state-of-the-art, our goal is to evaluate patient-specific features of IMR with a comprehensive analysis of the LVMV in the setting of surgical decision making.

The objective of this study is to automate and evaluate the accuracy of LVMV segmentation of 3D TEE images that are acquired pre-operatively in the operating room. Multi-atlas label fusion has proven successful for mitral valve segmentation even with a limited amount of data (i.e., 20 atlases) [5]. Given its previous success and that the LV and MV are relatively consistent in appearance in 3D TEE images acquired from adult patients, we hypothesize that the multi-atlas label fusion approach is an appropriate method for tackling this problem.

2 Methods and Materials

2.1 Materials

Data.—A total of 14 pre-operative real-time 3D TEE images were acquired at the Hospital of University of Pennsylvania. Of these, 8 images were acquired from patients with severe IMR and 6 were acquired from patients with normal MV functionality using a transesophageal matrix array transducer and the iE33 platform (Philips Healthcare). In this work, “normal” cases refer to patients who underwent cardiac surgery unrelated to the mitral valve and who have no morphological or functional abnormalities of the MV. In this study, image segmentation focused on the mid-systolic frame of the cardiac cycle, which has been shown to be valuable for predicting post-repair disease recurrence [4]. As a reference for evaluation of multi-atlas segmentation, manual segmentations were generated, and then finalized and reviewed by an expert cardiac surgeon (co-author YS). The manual and multi-atlas segmentations (see Fig. 1) include three labels: the anterior (red) and posterior (green) leaflets of the mitral valve and the left ventricular wall with the exclusion of trabeculae and papillary muscles (blue). In order to initialize atlas-based registration, 5 landmarks were identified in the mid-systolic frame. As seen in Fig. 1, these 5 landmarks consist of the anterior aortic peak (AAOP) of the annulus, anterior commissure (ACM), mid-posterior annulus (MPA), posterior commissure (PCM) and the midpoint of the coaptation zone (COAP). In this study, the commissures are defined as landmarks on the mitral annulus that are points of transition between the anterior and posterior leaflets. We approximate the commissures to be on the annulus since these points are most consistently identifiable in mid-systolic TEE images.

2.2 Multi-atlas Label Fusion

Given the limited data set and the consistency in LVMV appearance in 3D TEE, we can utilize multi-atlas label fusion (MALF) [8]. The MALF algorithm is composed of two steps: (1) registration of a collection of atlases to a target image to generate candidate segmentations and (2) joint label fusion of the registered atlas segmentations form the consensus multi-atlas segmentation. First, we register the atlases to a target image using a combination of affine and diffeomorphic transformations. The affine transformation is generated from user-defined landmarks, and the diffeomorphic transformation is calculated using the Advanced Normalization Tools (ANTs) diffeomorphic deformation framework [10]. We apply joint label fusion to combine the resulting candidate segmentations to form the consensus label map. Joint label fusion is particularly advantageous because it is a locally varying weighted voting scheme that optimizes voting weights based on similarities between the atlases and target image. These optimal voting weights account for similarities in the atlases themselves, which helps to reduce bias associated with redundancy in the atlas set. Figure 2 summarizes the multi-atlas pipeline.

3 Results

A leave-one-out evaluation was performed in order to assess the accuracy of the resulting segmentations. For each of the 14 semi-automated image segmentations performed, the images from the other 13 subjects were used as atlases for multi-atlas segmentation, and the

multi-atlas segmentation result was evaluated against the manual segmentation from the same subject. This process was performed for each subject. In order to evaluate reproducibility of the semi-automated method, we repeated this process for a set of target images that were initialized by a second observer.

The Dice coefficients with reference to the manual segmentations for all three individual labels and for the combined labels were used as the metric for comparison. From Tables 1 and 2, we see that while the Dice coefficients for each segmented label may vary, the performance of MALF is consistent. The average Dice coefficients for the anterior and posterior leaflets and LV across both experiments are 0.78 ± 0.04 , 0.74 ± 0.06 , 0.78 ± 0.05 , respectively. From Table 3, we see that when examining the inter-observer Dice coefficients (i.e., the overlap between the multi-atlas segmentations initialized by Observers 1 and 2) demonstrate high reproducibility in semi-automated segmentation. The average inter-observer Dice coefficients for the anterior and posterior leaflets and LV are 0.90 ± 0.02 , 0.90 ± 0.02 , 0.87 ± 0.06 , respectively.

Figure 4 plots the Dice coefficients with reference to manual segmentations for the multi-atlas and registered atlas segmentations. Figure 3 shows the “Dice box”, a qualitative summary of the overall Dice coefficients, which allows for evaluation of the registration of each atlas segmentation onto its target image. The presented Dice coefficients are calculated in reference to the expert manual segmentations of the target subject. Of note, the demonstrated Dice coefficients of the MALF segmentation is consistently greater when examining each row of the “Dice box”. This trend is quantitatively confirmed in Fig. 4.

4 Discussion

The ability to automatically generate accurate representations of the LVMV complex from 3D TEE images is a critical step towards predicting post-surgical outcomes of treatment for severe IMR in the operation room. Previous work has shown that geometric features such as left ventricular basal aneurysm had the highest predictive value ($AUC = 0.94$ [9] and $AUC = 0.83$ [3]) when combined with mitral valve-derived features. The automation of the segmentation is a significant contribution to accelerating intraoperative decision making and allowing for a more quantitative analysis of the LVMV complex in severe IMR for improving patient risk stratification.

Towards this goal, this work demonstrates promising results in semi-automated LVMV segmentation with average Dice scores of 0.78 ± 0.06 (all labels) and 0.79 ± 0.03 (excluding nrml01, an outlier) relative to manual segmentation. The method also has high reproducibility with average inter-observer Dice scores for the semi-automated combined LVMV segmentation of 0.87 ± 0.06 and 0.89 ± 0.02 (excluding nrml01). Atlas-based segmentation accuracy is related to the effectiveness of the registration of each atlas to the target image. The advantage of utilizing label fusion for combining the candidate segmentations of all atlases and correcting biases in the atlas set is clearly demonstrated in Fig. 4. Here, the MALF segmentations have the highest Dice coefficient values compared to the individual candidate segmentations. Overall the quality of the semi-automated segmentations was both quantitatively and qualitatively high (see Fig. 3) with the exception

of the segmentation of nrml01, which was the outlier of the group. For the nrml01 dataset, the average Dice coefficient of individual atlas registrations was 0.56 ± 0.15 and the Dice coefficient of the multi-atlas label fusion was 0.65. This was due to poor image quality caused by signal attenuation that led to a visibly occluded left ventricular apex region, as seen in Fig. 5. This problem could potentially be addressed in further studies by adding a template-based shape modeling component to the pipeline as discussed in [5], which has been shown to correct for missing components in some mitral valve segmentations.

The results of this study, which were produced with a limited dataset of 13 reference atlases, represents significant progress towards generating statistical atlases for further clinical analyses. The next step is to extract measurements and analyze the LVMV structure in terms of morphology. To capture the variations of the joint LVMV complex we could potentially utilize continuous medial representation (cm-rep), which is an excellent candidate for geometric modeling that has allowed for previous success in modeling the mitral valve accurately and for reliable feature extraction and statistical analysis [15,16]. Finally, the current algorithm is a CPU implementation and is not optimized in terms of speed, having a runtime of approximately 3 h. The runtime for the LVMV segmentation is much larger than that for the segmentation of the valve alone since the field of view is larger. This can be improved in the future by using a GPU implementation for the registration steps, which has been shown to decrease the runtime by a factor of 55 [11]. If successful, the combination of accurate segmentation and modeling will allow for more sophisticated morphometric measurements and, ultimately, a more informed decision in the immediate surgical setting.

In conclusion, multi-atlas segmentation with joint label fusion is a promising tool for segmentation of the LVMV from 3D TEE pre-operative images. Semi-automated segmentation was demonstrated both in patients with severe IMR and in patients with normal MV function using TEE images acquired in the pre-operative setting. In the future, we will fully automate the segmentation and employ geometric modeling for comprehensive morphological assessment of the LVMV complex.

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Fig. 1. (left) The left ventricle mitral valve manual segmentation with three components: anterior leaflet (red), posterior leaflet (green) and left ventricle (blue). (right) These 5 mitral valve anatomical landmarks are used for the affine transform initialization.

Fig. 2.

Multi-atlas label fusion pipeline shown. The first step uses the manual input of 5 landmarks on the target image followed by atlas registration to generate the candidate segmentations. The second step applies joint label fusion to output the multi-atlas segmentation.

Fig. 3.

Demonstrates a qualitative summary of registration performance and mean Dice coefficients across both experiments for each of the candidate segmentations, in order to highlight outliers.

Fig. 4.

Demonstrates a quantitative summary of the registration performance and mean Dice coefficients across both experiments for each of the candidate segmentations.

Fig. 5. nrml01 (top) image exhibits signal dropout (red arrow) leading to the poor registration of candidate segmentations that affect the multi-atlas segmentation. We can clearly see this in comparison to imr15 (bottom), which is a representative segmentation in the leave-one-out study.

Table 1.

Accuracy of multi-atlas segmentation initialized by Observer 1 with respect to expert manual segmentation

ID	Dice coefficients			Overall Dice
malf seg	Anterior leaflet	Posterior leaflet	Left ventricle	LVMV
imr 01	0.736	0.693	0.765	0.767
imr 02	0.746	0.626	0.764	0.767
imr 05	0.772	0.724	0.827	0.828
imr 06	0.785	0.777	0.824	0.825
imr 08	0.851	0.805	0.781	0.782
imr 09	0.839	0.813	0.759	0.761
imr 11	0.821	0.820	0.839	0.840
imr 15	0.843	0.783	0.810	0.812
nrml 01	0.798	0.770	0.584	0.588
nrml 03	0.774	0.714	0.790	0.792
nrml 04	0.683	0.666	0.800	0.801
nrml 06	0.760	0.726	0.752	0.754
nrml 07	0.790	0.777	0.811	0.812
nrml 08	0.777	0.794	0.786	0.788

Table 2.

Accuracy of multi-atlas segmentation initialized by Observer 2 with respect to expert manual segmentation

ID	Dice coefficients			Overall Dice
malf seg	Anterior leaflet	Posterior leaflet	Left ventricle	LVMV
imr 01	0.740	0.698	0.779	0.780
imr 02	0.762	0.599	0.765	0.768
imr 05	0.771	0.730	0.826	0.826
imr 06	0.762	0.776	0.841	0.841
imr 08	0.846	0.811	0.754	0.756
imr 09	0.847	0.830	0.762	0.764
imr 11	0.776	0.775	0.844	0.845
imr 15	0.780	0.752	0.769	0.772
nrml 01	0.764	0.743	0.703	0.705
nrml 03	0.771	0.711	0.776	0.778
nrml 04	0.674	0.663	0.800	0.800
nrml 06	0.756	0.731	0.724	0.727
nrml 07	0.756	0.738	0.800	0.800
nrml 08	0.791	0.802	0.789	0.791

Table 3.

Inter-observer Dice coefficients generated from the overlap between multi-atlas segmentations initialized by Observers 1 and 2

ID	Dice coefficients			Overall Dice
mal seg	Anterior leaflet	Posterior leaflet	Left ventricle	LVMV
imr 01	0.927	0.922	0.905	0.906
imr 02	0.890	0.869	0.880	0.881
imr 05	0.924	0.917	0.905	0.906
imr 06	0.892	0.889	0.897	0.898
imr 08	0.885	0.877	0.846	0.847
imr 09	0.916	0.904	0.907	0.907
imr 11	0.872	0.880	0.892	0.893
imr 15	0.856	0.864	0.841	0.843
nrml 01	0.893	0.869	0.674	0.679
nrml 03	0.923	0.915	0.888	0.889
nrml 04	0.920	0.918	0.901	0.901
nrml 06	0.912	0.905	0.879	0.880
nrml 07	0.875	0.871	0.885	0.885
nrml 08	0.936	0.933	0.930	0.931