LEFT VENTRICULAR EJECTION FRACTION: COMPARISON BETWEEN TRUE VOLUME-BASED MEASUREMENTS AND AREA-BASED ESTIMATES

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ABSTRACT

Left ventricular ejection fraction (LVEF) is a critical measure of cardiac health commonly acquired in clinical practice, which serves as the basis for cardiovascular therapeutic treatment. Ultrasound (US) imaging of the heart is the most common, least expensive, reliable and non-invasive modality to assess LVEF. Cardiologists, in practice, persistently use 2D US images to provide visual estimates of LVEF, which are based on 2D information embedded in the US images by examining the area changes in LV blood pool between diastole and systole. There has been some anecdotal evidence that visual estimation of the LVEF based on the area changes of the LV blood pool significantly underestimate true LVEF. True LVEF should be calculated based on changes in LV volumes between diastole and systole. In this project, we utilized both idealized models of the LV geometry — a truncated prolate spheroid (TPS) and a paraboloid model — to represent the LV anatomy. Cross-sectional areas and volumes of simulated LV shapes using both models were calculated to compare the LVEF. Further, a LV reconstruction algorithm was employed to build the LV blood pool volume in both systole and diastole from multi-plane 2D US imaging data. Our mathematical models yielded an area-based LVEF of $41 \pm 4.7\%$ and a volume-based LVEF of $55 \pm 5.7\%$, while the 3D reconstruction model showed an area-based LVEF of $35 \pm 11.9\%$ and a volume-based LVEF of $48.0 \pm 14.0\%$. In summary, the area-based LVEF using all three models underestimate the volume-based LVEF using corresponding models by 13% to 14%. This preliminary study confirms both mathematically and empirically that area-based LVEF estimates indeed underestimate the true volume-based LVEF measurements and suggests that true volumetric measurements of the LV blood pool must be computed to correctly assess cardiac LVEF.

Index Terms— echocardiography, 3D reconstruction, left ventricular ejection fraction

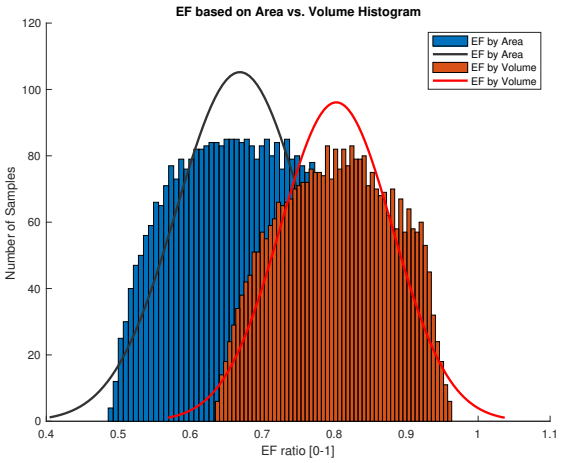

Fig. 1: Using TPS and parabolid models,area-based LVEFs significantly underestimate volume-based ones.

1. INTRODUCTION

LVEF is an effective biomarker for cardiac health and is considered one of the most vital measures in cardiology[1]. Therapeutic treatments on patients are often qualified by LVEF measures. Many hospital systems also use LVEF data as a metric for patient management and clinic trial eligibility assessment.

LVEF is defined as the ratio between the stroke volume (i.e., the difference between the left ventricular blood pool volume at end-diastole $V_{diastole}$ and end-systole $V_{systole}$) and the end-diastolic volume as illustrated by the equation below:

$$LVEF = \frac{V_{diastole} - V_{systole}}{V_{diastole}} = \frac{StrokeVolume}{V_{diastole}} \quad (1)$$

Cardiologists, however, most often use 2D US images to estimate EF visually based on the changes in area of the LV

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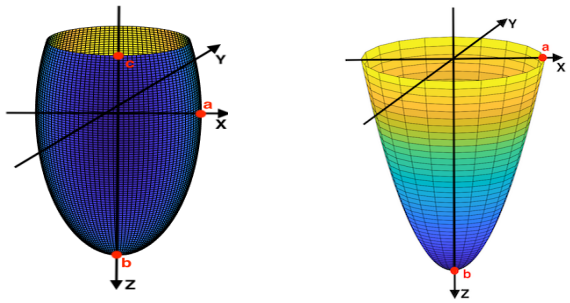
blood pools between end-diastole and end-systole rather than change in volumes. Galileo Galilei's "Square-Cube Law" states that the ratio of two volumes will always be greater than the ratio of their surfaces. Consequently, an object's change in three-dimensional space is always greater than its corresponding change two-dimensional space. Therefore, the practice in clinical setting is suspected to produce lower LVEFs than their true volumetric calculations.

A preliminary analysis conducted by our clinical collaborator on a database of 68 patients suggested that the LVEF estimates based on area changes are approximately 16.7% lower than the LVEF estimates based on volume changes. More interestingly, the comparison exposed that there is a bias for the visually estimated LVEF towards the lower values, in general, as cardiologists rather be safe than sorry. That is, if in doubt, patients would receive treatments to prevent potential cardiac malfunction even if they might appear unnecessary.

Another statistical characteristic of the visually estimated LVEFs is "binning". Visual estimations of LVEF are often reported as discrete numbers in increments of 5%, which is caused by the lack of denomination associated with the rough visual estimation. Such phenomenon is similar to determining the exact time on a clock without tick marks — an exact time to the minute would be difficult and imprecise, hence most reported readings would be aligned with 5-min intervals or even coarser. This "binning" characteristic is detrimental; for a healthy person, the LVEF should exceed 55%, while a LVEF below 35% is considered reduced contraction efficiency [2]. Therefore, when the visually estimated LVEFs are around the 55% or 35% thresholds, the coarse increment of reported values will easily qualify a patient for the incorrect category. Consequently, people without cardiac disease may be diagnosed with reduced LVEF and vice versa.

Therapeutic treatments often include expensive operations and the implantation of cardiac assistive devices. A device such as implantable cardiac defibrillator (ICD) is associated with an initial operation cost between $30,000 to $50,000 approximately, and a follow-up treatment on the order of $5,000 to $17,000 [3]. In addition to the significant healthcare cost, the patients life changes inevitably[4].

The premise of this work is founded on the existing anecdotal evidence that LVEF based on LV blood pool area changes significantly underestimate true volumetric measurements, and the contributions described here are two-fold: 1) demonstrate, using both mathematical models of the LV geometry, as well as patient-specific data, that 2D area-based LVEF measurements significantly underestimate 3D volume-based measurements and 2) propose a method to reconstruct the 3D LV blood pool in systole and diastole from 2D multi-plane images and assess it against a current method used in the clinic.



(a) The TPS model is described by three parameters, which measure the width $\mathbf{a}$ at semi-axis $\mathbf{x}$, lengths $\mathbf{b}, \mathbf{c}$ from axis $\mathbf{x}$ to the apex and the mitral valve base.

(b) A paraboloid model of the LV is characterized by two parameters descriptive of the length $\mathbf{b}$ from semi-axis $\mathbf{x}$ to the apex and width at semi-axis $\mathbf{x}$.

Fig. 2: Mathematical approximations of the LV geometry.

2. METHODS

2.1. Geometric Models

We first used mathematical models of the idealized LV geometry to study the difference between area- and volume-based estimations of LVEF. Researchers previously proposed several mathematical approximations of the LV geometry: cylindrical [5], truncated prolate spheroid (TPS) [6], and paraboloid [7] models. Of these, the TPS and paraboloid models matched more closely to the LV shapes observed in our US imaging data, so they were used for geometric simulations to characterize and describe the LV. Both models are characterized by the length and width of the LV in systole and diastole according to clinical knowledge about the heart size available from our US imaging data.

As illustrated by Figure 2a and 2b, TPS model is characterized by three parameters and the paraboloid model is characterized by two parameters. For the TPS model, parameter $\mathbf{a}$ defines the shorter x-axis domain, parameter $\mathbf{b}$ defines the longer z-axis domain, and parameter $\mathbf{c}$ defines the location along z-axis where the ellipsoid is truncated[8]. Similarly, the paraboloid model takes the same parameters $\mathbf{a}$ and $\mathbf{b}$ but not $\mathbf{c}$. The truncated section of the TPS model leads to significantly different cross-sectional areas and internal volumes from those described by the paraboloid for any given dimension. Using the information gathered from our image dataset, we ran simulations of TPS and paraboloid models to generate shapes that range from thin-elongated LVs to wide-short LVs in order to cover a variety of LV shapes. The corresponding LVEFs were calculated based on the simulated LV cross-sectional areas and volumes subnsequently.

2.2. Clinical Data

US images of 68 de-identified, retrospectively imaged patients were used for this study. Each patient dataset consists of three apical chamber views: a two-chamber (2C) view, a three-chamber (3C) view and a four-chamber (4C) view, with the exception of several patients for whom the 3C view was replaced with a parasternal long axis (PLEX) view. In addition, each image is accompanied by a endocardial LV trace in both systole and diastole outlined by an experienced cardiologist. Several measurements were also provided by the software employed (GE's EchoPac PC) including the length of the ventricle from apex to base, blood pool circumference, blood pool area, and blood pool volume (computed using the method of discs).

2.3. 3D Volume Reconstruction from 2D Multi-plane US Images and LVEF Estimation

In the clinic, US machines estimate LV blood pool volumes using the "method of discs" in each of the three views once the endocardial LV border was traced. In short, the method assumes that the left ventricle is axisymmetric about its long axis and approximates its volume by revolving each endocardial trace about the apex to mitral valve base line. Moreover, to account for the fact that the heart was depicted using three views more or less at 60° apart, the same axisymmetric volume is estimated from the other two views in both systole and diastole. Finally, a systolic and diastolic blood pool volume is estimated by averaging the three volumes approximated from each of the three views.

As an alternative method, which does not make any assumptions about the LV axisymmetry, we proposed a method that leverages the true geometry of the LV depicted by the three 2D tri-plane US images and their relative spatial location. Since each patient's heart was imaged in three tomographic views[9] located 60° apart, a 3D LV volume was reconstructed by first co-locating the LV apex from all views, then aligning the apex-to-mitral-valve-base line from the three views along the vertical axis, and lastly using spline contours to interpolate between the points on the endocardial border of the three views at the same altitude from the apex. Instead of the spline interpolation method, a convex hull fitting algorithm similar to that proposed by Dangi *et al.*[10] could be employed. Both approaches — the spline-based interpolation or convex hull fitting — yielded similar 3D LV volumes, with minimal differences.

Following the 3D blood pool volume reconstruction, we proceeded to estimate the LVEF using the cross-sectional area measurements from the three views in systole and diastole and comparing it to the LVEF computed using the reconstructed 3D LV blood volumes.

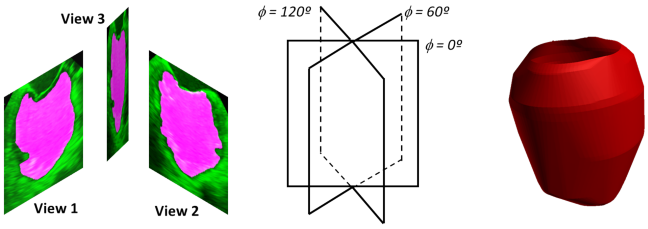
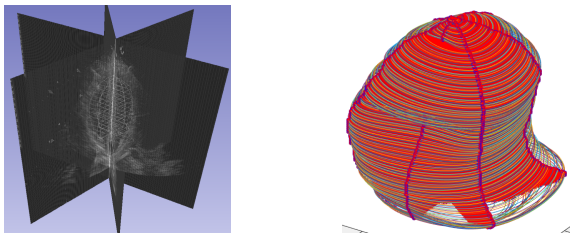


Fig. 3: 3D reconstruction workflow: extract LV blood pools in three views; align apices and mitral valve bases; reconstruction by convex hull interpolation between three views.



(a) Aligned images (b) Reconstructed volume

Fig. 4: LV volume reconstruction using convex hull model.

3. RESULTS

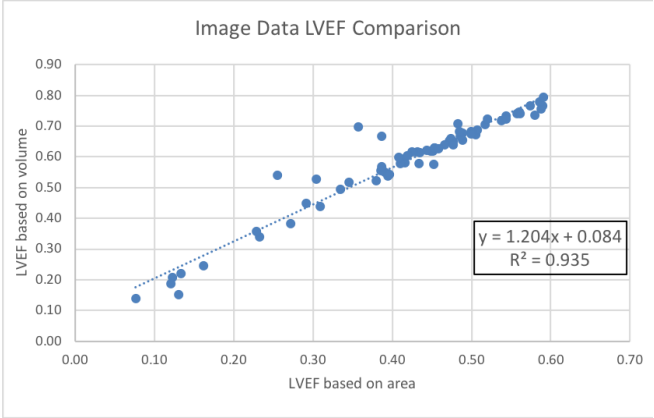
As observed from the retrospectively acquired and de-identified image database of 68 patients, the diameters of LV blood pools ranged from 1 cm to 4.5 cm and the lengths ranged from 2 cm to 14 cm. LV cross-sectional areas and volumes in both systole and diastole and the corresponding LVEFs were calculated for both idealized models across the whole range of heart sizes and geometries. Comparing the area- vs. volume-based LVEFs, both models clearly demonstrate that the area-based LVEF is significantly lower than the volume-based LVEF by approximately 16% on average. Volume-based LVEFs are higher than area-based ones across the lengths and radii of the LVs used to run the TPS and paraboloid model simulations. Further, the differences between volume-based and area-based LVEFs are higher for thin-elongated LV shapes than wide-short LV shapes using either geometric model. The Student's t test also confirmed that the area-based LEVF is significantly lower ($p < 0.05$) than the volume-based LVEF for all analyzed data.

Subsequently, the area- and volume-based LV measurements in both systole and diastole for our clinical data, TPS model, paraboloid model, and 3D reconstructed model were compared. As summarized in Table 1, the LVEF area and volume calculatioins are consistently different across all models. In all models, area-based LVEF calculations clearly underestimate the volume-based LVEF calculations for all models. Even though the mean and standard deviation of LVEFs based on TPS and paraboloid models were the same, both quan-

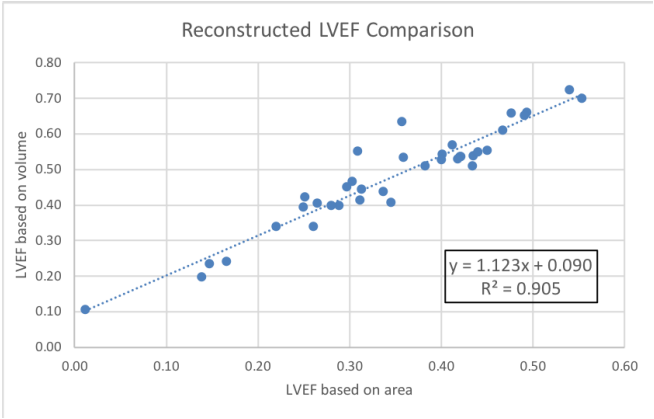
tities were produced from significantly different stroke and diastolic areas or volumes as shown in Table 1. Comparing the stroke and diastolic areas and volumes, the TPS model matched more closely to our reconstruction results from the US imaging data. The paraboloid model tends to overestimate the volume relative to the TPS model in the mid to apical range due to their different geometries. This observation also explains the limitations of using these idealized models to faithfully describe the LV geometry, but the TPS model is still considered a better approximation of the LV shape. Additionally, due to imperfect extraction of LV blood pools in our US images, the systolic areas and volumes were higher resulting in reduction in LVEFs. The volume-based values in the 'Clinical Data' column are not gold standard because they were calculated by GE software using method of disc volume estimation for each tomographic view without considering intricate variations in LV shapes between tomographic views.

Table 1: Summary statistics of the LVEF-related quantities based on the TPS model, paraboloid model, 3D LV reconstructions from the multi-plane 2D US imaging data, and the clinical data analysized using GE's EchoPac PC software.

Mean±Standard Deviation					
Quantity		Clinical Data	TPS Model	Paraboloid Model	Reconstruction Model
Stroke	Area $[cm^2]$	14 ± 4.1	16 ± 2.3	17 ± 3.8	12 ± 4.0
	Vol. $[ml]$	67 ± 20	100 ± 29	174 ± 35	62 ± 25
Diastolic	Area $[cm^2]$	35 ± 9.7	40 ± 10	43 ± 12	35 ± 10
	Vol. $[ml]$	127 ± 59	187 ± 73	317 ± 89	143 ± 76
LVEF	Area $[cm^2]$	42 ± 13	41 ± 4.7	41 ± 4.7	35 ± 12
	Vol. $[ml]$	59 ± 16	55 ± 5.7	55 ± 5.7	48 ± 14



(a) Image dataset results



(b) Reconstructed results

Fig. 5: Correlation between area- and volume-based LVEFs.

Note in Figure 5, the slopes and y-intercepts of the volume- vs. area-based regression curves yielded by the two methods — the EchoPac PC and the proposed method — are similar. Hence, both methods show the same difference between the the area- and volume-based LVEFs. The slight difference of line fitting variance between figure 5a and figure 5b is due to the variance introduced when manually extracting LV blood pools from expert-annotated LV blood pools in US imaging data to generate masks. These small errors add up when used to generate 3D reconstructed volumes.

4. CONCLUSION

We made the first attempt to quantitatively show, using both idealized mathematical models of the LV and patient specific US imaging data, that area-based LVEFs underestimate true volume-based LVEF calculations. Our findings demonstrate that no shortcut should be taken to determining the LVEF by any other means than calculating the blood pool volume in systole and diastole, such as relying on area changes as a surrogate for volume changes. It is necessary to calculate LVEFs based on volume changes to prevent patients from receiving inappropriate interventions or implantation of assistive devices duo to inaccurate LVEF estimations. Moreover, we also showed a method that utilizes the relative position and orientation of the multi-plane 2D US images to correctly reconstruct a more faithful representation of the LV blood pool than simply averaging three axisymmetric LV shapes. We will extend this study to build a statistical shape model of the LV based on the extended patient population, enabling us to study the effect of the orientation of the cross-sectional areas on the area-based LVEF estimates. Moreover, the statistical shape model will help reduce the intra- and inter-observer variability associated with the tracing of the LV endocardial border in both systole and diastole and also providing a more straightforward method to generate the LV volumes for LVEF calculations.

5. ACKNOWLEDGMENT

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