Published in final edited form as:

J Magn Reson Imaging. 2016 March ; 43(3): 585–593. doi:10.1002/jmri.25038.

The impact of end-diastolic and end-systolic phase selection in the volumetric evaluation of cardiac MRI

Francisco Contijoch, PhD, Walter RT Witschey, PhD, Kelly Rogers, BS, Joseph Gorman III, MD, Robert C Gorman, MD, Victor Ferrari, MD, and Yuchi Han, MD

Francisco Contijoch: fcont@seas.upenn.edu; Walter RT Witschey: witschey@mail.med.upenn.edu; Kelly Rogers: kellyrog@seas.upenn.edu; Joseph Gorman: Joseph.Gorman@uphs.upenn.edu; Robert C Gorman: robert.gorman@uphs.upenn.edu; Victor Ferrari: ferrariv@mail.med.upenn.edu; Yuchi Han: Yuchi.Han@uphs.upenn.edu

Abstract

Purpose—To evaluate the impact of end-diastolic (ED) and end-systolic (ES) cardiac phase selection methods since task force recommendation have neither provided quantitative evidence nor explored errors introduced by clinical shortcuts.

Materials and Methods—Multi-slice, short-axis cine images were collected in 60 clinical patients on a 1.5T scanner. User-initialized active contour segmentation software quantified global left ventricular (LV) volume across all cardiac phases. Different approaches for selection of (ED) and (ES) phase were evaluated by quantification of temporal and volumetric errors.

Results—For diastole, the mid-ventricular maximum slice volume coincided with maximum global volume in 82.1% of patients with ejection fraction (EF) $\geq 55\%$ ($p = 0.66$) and 71.9% of patients with EF $< 55\%$ ($p = 0.28$) and is an accurate approximation of maximum global volume while the first and last phases in a retrospectively ECG-gated acquisition introduced differences in cardiac phase selection ($p < 0.001$) which led to large errors in measured volume in some patients (12.7 and 10.1 mL, respectively). For systole, post-systolic shortening occurred in a significantly higher number of patients with EF $< 55\%$ (18.9%) compared to 3.6% of patients with EF $\geq 55\%$ ($p = 0.001$), which differentially impacted end-systolic volume estimation.

Conclusion—For end-diastolic phase selection, our results indicated that the use of the mid-ventricular slice volume maximum provided accurate volume estimates while selection of the first or last cardiac phase introduced differences in measured volume. For end-systolic phase, patients with EF $< 55\%$ had a higher prevalence of post-systolic shortening which suggests aortic valve closure should be used to estimate end-systolic volume.

Keywords

clinical cine MRI; post-systolic shortening; aortic valve closure

INTRODUCTION

Cine cardiovascular magnetic resonance imaging (MRI) is the accepted standard for quantification of ventricular volume and function (1). Measurement of end-diastolic (ED) and end-systolic (ES) volumes to obtain stroke volume (SV) and ejection fraction (EF) is an important element of any cardiac MRI evaluation and it is well known that different methods of calculating left ventricular (LV) volume can impact reported values (2, 3). Importantly, the selection of ED and ES phases has recently been reported to impact regional measures such as strain (4).

Expert documents have been developed to attempt to standardize volumetric evaluation in cardiac MRI. One element of these documents is the recommendation on how to select the ED and ES phases for subsequent quantification. The 2013 Task Force on Standardized Post Processing states that the ED and ES phases be identified as those “with the largest and smallest global LV blood volume” (1). This recommendation presents a practical problem; although the largest and small global LV volumes may be the desired ED and ES volumes, it is impossible to assess which cardiac phase corresponds to the maximum and minimum volume without performing segmentation on all the phases in all the slices. Although automated methods have emerged, none have adequately replaced human selection in clinical practice.

An earlier publication describes a simplified approach: Visually identify when a mid-ventricular slice achieves maximum and minimum volume and utilize it as a surrogate for when the entire LV achieves maximum and minimum volume (5). Since cine MRI acquisitions are ECG-gated, the first cardiac phase in the acquisition is often defined as end-diastole by default (6). However, the accuracy of either of these simplifications and the potential impact on measured hemodynamics have not been quantitatively evaluated

Furthermore, selecting the global LV minimum volume as the ES phase fails to account for potential post-systolic shortening (decrease in LV volume after aortic valve closure which does not contribute to stroke volume). Post-systolic shortening has been known to occur in healthy patients and can become more pronounced in patients with dyssynchrony (7). Echocardiographic evaluation of LV dyssynchrony uses 2-chamber, 4-chamber, and 3-chamber views which allow for identification of the aortic valve closure relative to cardiac motion. However, MRI-based assessment of LV function does not utilize 3-chamber images and the use of aortic valve closure to identify end-systole was proposed in the 2013 Task Force recommendation, but its use was recommended only in the presence of arrhythmia or mitral regurgitation (4). The volumetric impact of using the minimum global LV volume as the ES phase in patients with post-systolic shortening has not been well characterized.

In this work, we sought to evaluate the impact of end-diastolic and end-systolic cardiac phase selection methods and associated volumetric differences.

MATERIALS AND METHODS

Patients

Sixty consecutive patients scanned for clinical MRI between September 2012 and July 2013 were included in our study. These clinical patients were referred to evaluate non-ischemic cardiomyopathy or new onset of heart failure ($n = 29$), ischemic cardiomyopathy or assessment of coronary artery disease ($n = 6$), hypertrophic cardiomyopathy ($n = 5$), disorders of rhythm (ventricular tachycardia/premature ventricular contractions/left bundle branch block/complete heart block ($n = 11$), valvular heart disease ($n = 3$), pulmonary hypertension ($n = 2$), family history of cardiomyopathy ($n = 2$), syncope ($n = 1$), and coarctation ($n = 1$). 21 of these patients had prolonged QRS duration (> 120 ms) based on electrocardiogram.

A complete short-axis cine stack and visualization of the aortic valve opening (AVO) and closure (AVC) in the long-axis view were the only criteria used for inclusion in the study. The retrospective analysis was approved by our Institutional Review Board with waiver of consent and characteristics of the patient population are shown in Table 1.

Image Acquisition

MRI was performed on a single 1.5 T clinical imaging system (Avanto, Siemens Healthcare, Erlangen, Germany) equipped with nominal 40 mT/m magnetic field gradients, body RF transmit and a 16-channel, anterior and posterior RF receiver array.

Cine MRI was obtained using a conventional 2D, breath-held, multi-slice, retrospectively-gated, balanced steady-state free-precession sequence with the following imaging parameters, TE = 1.12 – 1.31 ms, flip angle = $51 - 82^\circ$, matrix = $144 - 192 \times 192$, field-of-view = $195 - 360$ mm $\times$ $240 - 400$ mm, bandwidth = 930 Hz/pixel, phases = 30, slices = 11–15, slice thickness = 8 mm, skip = 2 mm and temporal resolution = 30 – 45 ms. Short-axis images spanning the LV as well as left ventricular outflow tract (LVOT) images visualizing the aortic valve were obtained.

User-Initialized Active Contour Endocardial Segmentation (ACS)

Segmentation of cine images was performed through user-initialized active contour segmentation which has been shown to provide slice volume values comparable to manual segmentation using clinical tools (8, 9). Briefly, 2D image data was arranged in a 3D stack $N_x \times N_y \times N_t$ in open-source software (ITK-SNAP, University of Pennsylvania, Philadelphia, PA) with a typical size $192 \times 146 \times 90$ (Figure 1) (10). To minimize edge effects of the region growing, the cine images were concatenated in MATLAB (The MathWorks, Natick, MA) resulting in three times the number of cardiac phases ($N_t = 3 \times 30 = 90$). Intensity thresholding was used to generate a set of feature images of the LV intraventricular volume. Ventricular segmentation was initialized using a $3 \times 3 \times N_t$ pixel column centered in the ventricle and 3D active contour segmentation was performed using region competition with user-defined balloon and curvature forces (11). The advantage of this arrangement is temporally consistent and smooth LV volume data. Papillary muscles were excluded from the segmentation by the region-growing algorithm and manual

correction (if necessary) such that the LV blood volume was quantified. The basal slice was determined by identification of the slice in the short-axis stack with the mitral valve annular plane at end-systole. LV slice volume was quantified from segmented data using the pixel size. The global volume curve was obtained by summation of LV slice volumes obtained in selected slices. Using ACS, segmentation takes approximately 2 minutes for a single slice and 20 minutes for the entire LV (all slices and all phases).

Estimation of ED and ES Volume

Several different approaches for selection of ED and ES were evaluated. In the Grover et al, the cardiac phase of mid-ventricular slice volume maximum was utilized to estimate the global maximum volume (5). However, clinically, the first or last cardiac phase in a retrospectively-gated cine MRI acquisition is often utilized as the ED phase (6). We evaluated these three approaches (mid-ventricular slice volume maximum, first, and last cardiac phase) by finding the distribution of slice phases when maximum global volume is achieved. In addition, the volumetric error generated by utilizing these approaches was calculated. For example, the volumetric error for end-diastole was calculated as the Global Volume Maximum – “volume determined using another approach” and the values were reported as a mean and standard deviation.

Two approaches for the selection of end-systole have been proposed. We quantified the volume difference associated with the use of a mid-ventricular slice to identify end-systole compared to the global minimal volume. The difference was quantified both in terms of timing and volume. Since, both the mid-ventricular slice and the minimum global volume approaches are sensitive to post-systolic shortening, we utilized the occurrence of aortic valve closure to evaluate the volumetric difference due to post-systolic shortening. We again evaluated the difference (timing and volume) associated with use of the mid-ventricular slice as well as the minimum global volume in relation to the cardiac phase when the aortic valve closes.

Quantitative analysis was performed separately on patients with high EF ($\geq 55\%$, $n=28$) from those with EF $< 55\%$ ($n=32$) to evaluate if the observed errors in volume estimation were function-dependent (12).

Quantification of Post-Systolic Shortening

ES volume may be underestimated when measured utilizing the minimum global volume if substantial post-systolic shortening (PSS) is present. We investigated the observed phase and volumetric difference between the aortic valve closure (AVC) phase and the minimum global volume phase. Normal AVC was defined as occurring within 1 cardiac phase of the minimum global volume while post-systolic shortening was defined as aortic valve closure occurring more than one frame prior to global volume minimum and late aortic valve closure was defined as occurring more than one frame after global volume minimum.

Statistical Analysis

For all parameters, the means $\pm$ standard deviations of continuous data were calculated. Normality was checked and subsequently two-tailed paired Student's t-tests ($p < 0.05$) were

performed to detect significant differences in both the cardiac phase and the volume measurements. Univariate logistic regression was performed to assess parameters for early aortic valve closure. Although the clinical significance of measured error in volume and ejection fraction depends on the clinical question, volumetric errors < 2 mL and ejection fraction errors < 1% were considered insignificant as they fall within the previously reported range of intra- and interobserver variability (12).

RESULTS

Using ACS, the entire LV volume curve throughout the cardiac cycle was visualized (Figure 2) and the global maximum and minimum volumes were reliably identified. In some patients, the different approaches yielded exactly the same phases and volumes (Figure 2A) while in others, large differences are observed in the different approaches (Figure 2B and 2C).

Distribution of Global Volume Maximum

Histograms of the occurrence of maximum global volume as a function of the cardiac cycle in patients with EF ≥ 55% as well as with EF < 55% are shown in Figure 3A and 3C. As shown in Table 2, in patients with EF ≥ 55%, the first cardiac phase coincided with the maximum global volume in only 2 of 28 patients (7.1%) while the last cardiac phase coincided with maximum global volume in 16 of 28 patients (57.1%) (Figure 3A). The remaining 10 patients (35.7%) had the global maximum value occurring during the end of the image series but prior to the last cardiac phase. This distribution of phases was statistically significantly different from the first cardiac phase ($p < 0.001$).

The impact of these approaches on estimated EDV is shown in Figure 3B and Table 2. In patients with EF ≥ 55%, the first phase underestimated ED volume by 2.8 ± 2.3 mL ($p < 0.001$) with a maximum difference of 8.0 mL. The last cardiac phase reduced this difference to 0.9 ± 1.5 mL ($p < 0.001$, maximum difference = 6.3 mL). This reduction was statistically significant ($p=0.001$). However, in both approaches there were patients with large differences (> 5mL) in measured ED volume ($n=5$ using first phase and $n=1$, using last phase).

In patients with EF < 55% (Figure 3C and Table 2), the first cardiac phase coincided with the maximum global volume in 7 of 32 patients (21.9%) while the last cardiac phase coincided with maximum global volume in 7 of 32 patients (21.9%). 3 patients (9.4%) had the global maximum value occurring after the first phase and 15 patients (46.9%) had the global maximum value occurring during the end of the image series but prior to the last cardiac phase. This distribution of phases was statistically significantly different from the first cardiac phase ($p < 0.001$).

The impact of these approaches on estimated EDV in patients with EF < 55% is shown in Figure 3D and Table 2. The first phase underestimated ED volume (2.4 ± 2.7 mL, $p < 0.001$) with a maximum difference of 12.7 mL. The last cardiac phase reduced this difference (1.5 ± 2.0 mL, $p < 0.001$, maximum error = 10.1 mL). This reduction was statistically significant ($p=0.015$). The low mean difference was due to exact agreement in cardiac phase in 21.9%

of patients for both the first and last cardiac phase. However, both approaches had two patients with large differences ($> 5\text{mL}$) in measured ED volume.

Use of the Mid-Ventricular Slice Volume Maximum for ED Phase Estimation

In patients with $\text{EF} \geq 55\%$, the mid-ventricular slice volume maximum occurred in close proximity to the maximum global volume (Table 2). In 82.1% of patients ($n=23$ of 28), there was exact agreement between the two approaches. As a result there is no statistically significant difference in the ED phase selected using the mid-ventricular slice volume in comparison to the global volume ($p = 0.66$). The use of the mid-ventricular slice maximum, led to small differences in EDV ($0.1 \text{ mL} \pm 0.3 \text{ mL}$, $p=0.046$), which were statistically significant (Figure 3B and Table 2), but clinically negligible. The approach also decreased the maximum observed difference (1.2 mL).

In patients with $\text{EF} < 55\%$, the mid-ventricular slice volume maximum also occurred in close proximity to the maximum global volume (Table 2). In 71.9% of patients ($n=23$ of 32), there was exact agreement between the two approaches. As a result there is no statistically significant difference in the ED phase selected using the mid-ventricular slice volume in comparison to the global volume ($p = 0.28$). The use of the mid-ventricular slice maximum, led to a small underestimation in EDV ($0.3 \text{ mL} \pm 0.9 \text{ mL}$, maximum observed difference = 4.5 mL , Figure 3D and Table 2), which was not statistically significant ($p=0.055$).

ES Phase Selection

In patients with $\text{EF} \geq 55\%$, the minimum global volume coincided with the mid-ventricular slice volume minimum in 21 of 28 patients (75.0%). 5 patients (17.9%) had the mid-ventricular slice minimum occurring before minimum global volume and 2 (7.1%) had mid-ventricular slice minimum after minimum global volume (Table 2). The differences in ES phase identified were not statistically significant ($p = 0.76$). Using the mid-ventricular slice volume results in higher estimate of ES volume $0.5 \pm 1.0 \text{ mL}$ (Table 2) with a maximum difference of 2.8 mL ($p=0.01$).

In patients with $\text{EF} < 55\%$, the minimum global volume coincided with the mid-ventricular slice volume minimum in only 8 of the 32 patients (25.0%) with 10 patients having mid-ventricular slice minimum occurring before and 14 patients having the mid-ventricular slice minimum occurring after the global volume minimum (Table 2). The difference in phase selected was not statistically significant ($p = 0.08$). ES volume was higher by $0.9 \pm 0.8 \text{ mL}$ (Table 2) with a maximum difference of 3.1 mL ($p<0.001$).

Post-Systolic Shortening Effects

Table 3 summarizes the results found regarding post-systolic shortening. In patients with $\text{EF} \geq 55\%$, AVC was within one phase of the minimum global volume in 25 of the 28 (89.3 %) patients. PSS occurred in one (3.6%) patient and late aortic valve closure in two (7.1%) of patients. In patients with $\text{EF} < 55\%$, AVC was within one phase of the minimum global volume in 25 of the 32 (78.1 %) patients. PSS occurred in six (18.9%) patients and late aortic valve closure occurred in one (3.1%) patient.

The difference in measured ES volume based on aortic valve timing is shown in Table 3 and Figure 4A (EF $\geq 55\%$) and 4B (EF $< 55\%$). Normal aortic valve closure (within one frame of global volume minimum) resulted in small differences in ES volume in patients with EF $\geq 55\%$ (0.8 ± 1.1 mL, $n = 25$) as well as EF $< 55\%$ (0.4 ± 0.7 mL, $n=25$). We observed post-systolic shortening of 8.0 mL ($n=1$) in patients with EF $\geq 55\%$, and 3.7 ± 4.5 mL ($n=6$) in patients with EF $< 55\%$. Late aortic valve closure led to slightly higher estimates of ES volume in patients with EF $\geq 55\%$ (1.9 ± 1.4 mL, $n=2$) as well as EF $< 55\%$ (1.0 mL, $n=1$).

Derived Measures of Cardiac Function

Although the differences reported using different approaches for ED and ES volume are often small individually, clinical measures of function such as SV and EF are calculated by combining these two estimates. As a result, larger differences were seen for some patients (Table 4).

In patients with EF $\geq 55\%$, using the first phase as end-diastole and the mid-ventricular slice volume minimum for end-systole underestimated the SV by 3.3 ± 2.7 mL, maximum difference = 9.2 mL ($p < 0.001$) which led to an underestimation of EF of $1.6 \pm 1.7\%$, maximum difference = 6.7% ($p < 0.001$). The use of the last phase for end-diastole improved the estimate of SV (underestimation = 1.4 ± 1.7 mL, maximum difference = 6.3 mL, $p < 0.001$) as well as the EF (underestimation = $0.9 \pm 1.4\%$, maximum difference = 5.5%, $p < 0.001$). Furthermore, using the mid-ventricular slice volume maximum to define end-diastole further improved the accuracy of SV (underestimation = 0.6 ± 1.0 mL, maximum difference = 2.8 mL, $p < 0.001$) and EF (underestimation = $0.6 \pm 1.3\%$, maximum difference = 5.5%, $p < 0.001$).

We also calculated the differences in measurements for patients with EF $< 55\%$, the use of the first phase for end-diastole and mid-ventricular slice volume minimum for end-systole underestimated SV by ± 2.9 mL, max difference = 13.6 mL, ($p < 0.001$) which led to an underestimation of EF of $1.3 \pm 1.0\%$, maximum difference = 4.0%, ($p < 0.001$). In patients with EF $< 55\%$, the use of the last phase did not significantly change the estimate of SV (underestimation = 2.4 ± 2.2 mL, max difference = 11.1 mL, $p < 0.001$) and had a small effect on EF (underestimation = $1.0 \pm 0.8\%$, maximum difference = 3.2%, $p < 0.001$). The use of the mid-ventricular slice volume maximum to define end-diastole improved the accuracy of both SV (underestimation = 1.2 ± 1.5 mL, max difference = 7.3 mL, $p < 0.001$) and EF (underestimation = $0.5 \pm 0.8\%$, maximum difference = 3.6%, $p < 0.001$).

Analysis comparing patients with normal QRS duration to those with prolonged QRS duration did not demonstrate any statistically significant differences in measured differences (p -values > 0.21).

Parameters Associated with PSS

In our patient population, 21 patients had prolonged QRS duration due to a left bundle branch block ($n=10$), bifascicular block ($n=5$), right bundle branch block ($n=4$), Wolff-Parkinson-White syndrome ($n=1$), and non-specific interventricular conduction delay ($n=1$). Categorizing patients based on EF and QRS duration indicated a different prevalence in PSS. In patients with EF $\geq 55\%$, no PSS was observed in patients with normal QRS duration

(n=16) and one case of PSS (with RBBB) was observed amongst patients with prolonged QRS duration (1 of 12, 8%). In patients with EF < 55%, PSS was observed in 4 of 23 (17%) patients with normal QRS duration and 2 of 9 (22%) patients with prolonged QRS.

Univariate logistic regression of early aortic valve closure and PSS using age, sex, body surface area (BSA), QRS duration, LVEDV, indexed LVEDV to BSA, and LVEF did not yield any significant parameters in our cohort.

DISCUSSION

Different methods have been used for ED and ES phase selection including the use of the mid-ventricular slice to establish reference values for volumetric data (5). We have found that the maximum global volume often occurred during a cardiac phase other than the first or last in a ECG-gated retrospective acquisition. As a result, using the first or last cardiac phase to estimate EDV led to consistent underestimations. In several patients, there were large (>5 mL) underestimations of EDV, regardless of EF. Identifying the maximum volume observed in a mid-ventricular slice as the end-diastolic phase mitigated these errors. Specifically, the approach increased identification of the correct ED cardiac phase, decreased the volumetric error in EDV, and, eliminated large underestimations.

Identification of the end-systolic phase by identifying the minimum volume of a mid-ventricular slice provided a fairly accurate method for estimation of global volume minimum in patients with EF ≥ 55% and EF < 55%. However, identifying the global volume minimum led to an underestimation of ESV in the setting of post-systolic shortening, which we found to be more prevalent in patients with EF < 55%.

The errors in estimation of end-diastolic and end-systolic volume lead to errors in stroke volume and ejection fraction estimates, which are both improved using the mid-ventricular slice to identify the correct cardiac phases.

Although the 2013 Task Force on Standardized Post Processing has recommended ED and ES phases be identified as those “with the largest and smallest global LV blood volume”, the practical implementation of this without complete tracing of all phases and all slices is challenging. In one study, by Maceira et al, which sought to “define ranges for normal left ventricular volumes and systolic/diastolic function” the method to select ED and ES phase was not standardized since “since there was no requirement to choose the largest and smallest ventricular frames” (13). As a result, it is unclear in what percentage of patients the EDV and ESV corresponded to the largest and smallest ventricular volume. Furthermore, the method used to select the ED and ES phase in each patient is not described.

For end-diastole, our results showed that choosing the first or last phase in a retrospectively-gated cine MRI acquisition without going through all the phases did not adequately approximate maximum volume, especially the first-phase approach. However, the phase corresponding to mid-ventricular slice maximum volume was approximation for the phase of maximum global volume. This was true for patients regardless of their EF.

For ES volume approximation, the different approaches (minimum global volume, mid-ventricular slice minimum volume, and aortic valve closure) did not lead to significant differences in the measured ES cardiac phase in patients with EF $\geq 55\%$. In these patients, the use of the mid-ventricular slice volume minimum resulted in a slightly higher estimate of ESV when compared to minimum global volume which was statistically significant, but likely not clinically significant due to the intra- and interobserver variability previously described using SSFP MRI (12).

In patients with EF $< 55\%$, there was a statistically significant difference in the measured ES volume using mid-ventricular minimum volume compared to global minimum volume. However, the difference in global volume was small and may not be clinically significant. The presence of systolic dysfunction appears to make the use of a mid-ventricular slice to identify the global volume minimum more challenging.

Identifying the aortic valve closure phase allows for quantification of the volumetric effect of post-systolic shortening (7, 15). Most patients in our study (regardless of EF) had aortic valve closure occurring within one frame of the global volume minimum. However, in some patients, there was considerable post-systolic shortening. The amount of shortening decreased with decreased EF and this may be due to a flattening of peak systole in the volume curve. In patients with high EF, there is likely a larger decrease in volume per frame during ejection, which led to a higher measured post-systolic shortening when compared to patients with low EF. However, more patients are necessary to further quantify this effect across different pathological states.

Although the effect of early or late aortic valve closure on measured end-systole was quantified in our patient population, predictors for early aortic valve closure could not be identified in our sample, likely due to small sample size. A larger study will be needed to characterize the subjects for whom aortic valve closure will be needed to accurately identify ES volume.

In our population, 21 patients had prolonged QRS duration (>120 ms). However, subanalysis of these patients did not result in significant differences in the accuracy of SV or EF relative to patients with normal QRS duration, which may be due to the low power of the subanalysis. Furthermore, despite a longer QRS duration, the prevalence of LV dyssynchrony may be low. The impact of ES phase selection would need to be explored further in a dedicated study of patients with prolonged QRS and LV dyssynchrony.

One general limitation of LV quantification techniques is the sensitivity of measurements to the choice of the basal slice. The ACS quantification was performed on slices that would otherwise be segmented using manual contouring (9). The choice of the basal slice was therefore based on visual identification of the mitral valve annular plane at end-systole. However, different criteria for identification of the basal slice would alter the volume curve and could lead to potential differences in measured ED and ES volumes.

Another limitation of the current work is the relatively small sample size. Additional patients with prolonged QRS duration and increased LV dyssynchrony could improve

understanding in these sub-populations. However, prior studies have used similar patient populations (n=60) in a single scanner retrospective study (12).

In conclusion, our results indicate that the use of the mid-ventricular slice maximum and minimum volume phase to estimate the global ED maximum and ES minimum volume is accurate in a range of clinical patients. However, the common clinical shortcut of using first and last phase does not yield equivalent results and should be avoided. For end-systole, different techniques evaluated result in small differences in measured volume. Post-systolic shortening can lead to difference in measure end-systolic volume in patients with decreased EF.

Acknowledgments

Grant Support: National Institute of Health: F31-HL120580, R00-HL108157, R01-EB014346, R01-HL103723, R01-HL63954, T32-HL007954, T32-EB009384

References

1. Schulz-Menger J, Bluemke DA, Bremerich J, et al. Standardized image interpretation and post processing in cardiovascular magnetic resonance: Society for Cardiovascular Magnetic Resonance (SCMR) board of trustees task force on standardized post processing. *J Cardiovasc Magn Reson*. 2013; 15:35. [PubMed: 23634753]
2. Weinsaft JW, Cham MD, Janik M, et al. Left ventricular papillary muscles and trabeculae are significant determinants of cardiac MRI volumetric measurements: effects on clinical standards in patients with advanced systolic dysfunction. *Int J Cardiol*. 2008; 126:359–365. [PubMed: 17698216]
3. Miller, Ca; Jordan, P.; Borg, A., et al. Quantification of left ventricular indices from SSFP cine imaging: impact of real-world variability in analysis methodology and utility of geometric modeling. *J Magn Reson Imaging*. 2013; 37:1213–1222. [PubMed: 23124767]
4. Mada RO, Lysyansky P, Daraban AM, Duchenne J, Voigt J-U. How to Define End-Diastole and End-Systole? Impact of Timing on Strain Measurements. *JACC Cardiovasc Imaging*. 2015; 8:148–157. [PubMed: 25577447]
5. Grover S, Leong D, Selvanayagam J. Evaluation of left ventricular function using cardiac magnetic resonance imaging. *J Nucl Cardiol*. 2011:351–365. [PubMed: 21234827]
6. Kunz RP, Oellig F, Krummenauer F, et al. Assessment of left ventricular function by breath-hold cine MR imaging: Comparison of different steady-state free precession sequences. *J Magn Reson Imaging*. 2005; 21:140–148. [PubMed: 15666401]
7. Voigt J. Incidence and characteristics of segmental postsystolic longitudinal shortening in normal, acutely ischemic, and scarred myocardium. *J Am Soc Echocardiogr*. 2003; 16:415–423. [PubMed: 12724649]
8. Witschey WRT, Contijoch F, McGarvey JR, et al. Real-Time Magnetic Resonance Imaging Technique for Determining Left Ventricle Pressure-Volume Loops. *Ann Thorac Surg*. 2014; 97:1597–1603. [PubMed: 24629301]
9. Contijoch F, Witschey WR, Rogers K, et al. User-Initialized Active Contour Segmentation and Golden-angle Real-Time Cardiac MRI Enable Accurate Assessment of LV Function in Patients with Sinus Rhythm and Arrhythmias. *J Cardiovasc Magn Reson*. 2015; 17 In Press.
10. Yushkevich PA, Piven J, Hazlett HC, et al. User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *Neuroimage*. 2006; 31:1116–1128. [PubMed: 16545965]
11. Zhu S, Yuille A. Region Competition: Unifying Snakes, Region Growing, and Bayes/MDL for Multiband Image Segmentation. *IEEE Trans Pattern Anal Mach Intell*. 1996; 18

12. Alfakih K, Plein S, Thiele H, Jones T, Ridgway JP, Sivananthan MU. Normal human left and right ventricular dimensions for MRI as assessed by turbo gradient echo and steady-state free precession imaging sequences. *J Magn Reson Imaging*. 2003; 17:323–329. [PubMed: 12594722]
13. Maceira AM, Prasad SK, Khan M, Pennell DJ. Normalized left ventricular systolic and diastolic function by steady state free precession cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2006; 8:417–426. [PubMed: 16755827]
14. Natori S, Lai S, Finn JP, et al. Cardiovascular function in multi-ethnic study of atherosclerosis: Normal values by age, sex, and ethnicity. *Am J Roentgenol*. 2006; 186 SUPPL. A(6)
15. Asanuma T, Nakatani S. Myocardial ischaemia and post-systolic shortening. *Heart*. 2015; 101:509–516. [PubMed: 25595416]

Figure 1.

User-initiated automated contour endocardial segmentation (ACS) for MRI images. The short-axis image is shown in the top row. The second and third rows illustrate projections along time illustrating three cardiac cycles. **A:** Image sequences are loaded as 3D volumes (2D+t) into software. **B:** The user defines an intensity threshold, which defines the endocardial border and results in a feature image. **C:** Region growing is then performed inside the feature image. **D:** The resulting segmentation can be manually corrected for any errors and quantification of the red region in each frame using the pixel volume is used to estimate slice volume. Global volume is obtained by summation of short-axis slice volume estimates.

Figure 2.

Global volume over time curve for three patients. The cine has been concatenated to allow for observation of the cyclical nature. The grey box outlines a single cardiac phase based on QRS triggering. The global volume maximum and minimum are labeled with red vertical lines. The maximum and minimum volume observed on a mid-ventricular slice are shown with purple triangles. For diastole, the first and last phase of the cine images are shown with green triangles while the aortic valve closure is shown with a green triangle in systole. For Patient 1, there is close agreement between the different approaches used for selection of ED and ES volume. Patient 2 illustrates the potential for differences in ED phase selection. The mid-ventricular slice maximum volume occurs prior to the global maximum volume and the first or last cardiac phase. Patient 3 illustrates the potential differences in systolic phase. Notably, aortic valve closure occurred prior to global volume minimum and the mid-ventricular slice minimum volume occurred after global volume minimum.

Figure 3.

Differences in measured ED phase and volume using proposed schemes in patients with normal EF (A – B) and EF < 55% (C – D). **A, C:** Measuring the global volume maximum (GVM) results in a distribution of phases. The first (red dotted line) and last (black dotted line) cardiac phases are shown with vertical lines. **B, D:** The volumetric error associated with the three approaches is shown with mid-ventricular maximum having the least volumetric error.

Figure 4.

Volume difference between minimum global volume and aortic valve closure as a function of aortic valve closure timing in patients with normal EF (**A**) and EF < 55% (**B**). **A:** In patients with EF $\geq$ 55%, early aortic valve closure led to post-systolic shortening in a single patient (QRS duration: 142 ms). Both normal (n=25) and late aortic valve closure (n = 2) showed small differences with the global volume minimum. **B:** In patients with EF < 55%, the prevalence of post-systolic shortening increased (n = 6) and the observed volume differences were higher than that observed with normal (n = 25) and late aortic valve closure (n = 1).

Table 1

Patient Characteristics

	Subjects		p-value
	EF 55% (n=28)	EF < 55% (n=32)	
Age (years)	50.9 ± 15.5	46.9 ± 16.5	0.337
Sex (male)	53.6%	65.6%	0.344
BSA (m ²)	1.76 ± 0.12	1.73 ± 0.09	0.370
QRS (ms)	115 ± 24	105 ± 25	0.179
EF* (%)	67.1 ± 8.5	34.0 ± 12.9	<0.001
LV EDV (ml)	99.7 ± 33.5	192.8 ± 63.7	<0.001
LV ESV (ml)	34.1 ± 16.4	132.6 ± 63.6	<0.001

* EF is evaluated using maximum and minimum global volumes.

Table 2

Occurrence of global volume maximum and global volume minimum in the cardiac cycle in patients with EF 55% and EF < 55%.

	EF 55%			EF < 55%		
	Prevalence	Volume Error - mL	p-value	Prevalence	Volume Error - mL	p-value
First Cardiac Phase	2/28 (7.1%)	2.8 ± 2.3 (max: 8.0)	< 0.001	7/32 (21.9%)	2.4 ± 2.7 (max: 12.7)	< 0.001
After First Cardiac Phase	0/28 (0%)			3/32 (9.4%)		
Last Cardiac Phase	16/28 (57.1%)	0.9 ± 1.5 (max: 6.3)	< 0.001	7/32 (21.9%)	1.5 ± 2.0 (max: 10.1)	< 0.001
Prior to Last Cardiac Phase	10/28 (35.7%)			15/32 (46.9%)		
Mid-Ventricular Slice Maximum Phase	23/28 (82.1%)	0.1 ± 0.3 (max: 1.2)	0.046	23/32 (71.9%)	0.3 ± 0.9 (max: 4.5)	0.055
Prior to Mid-Ventricular Slice Minimum	5/28 (17.9%)			10/32 (31.3%)		
Mid-Ventricular Slice Minimum	21/28 (75.0%)	0.5 ± 1.0 (max: 2.8)	0.01	8/32 (25.0%)	0.9 ± 0.8 (max: 3.1)	< 0.001
After Mid-Ventricular Slice Minimum	2/28 (7.1%)			14/32 (43.8%)		

* Volume Error is calculated as Global Volume Maximum – Proposed Method for EDV and as Proposed Method – Global Volume Minimum for ESV.

Table 3

Occurrence of post-systolic shortening and associated volume estimation of ESV

	EF ≥ 55%		EF < 55%	
	Prevalence	Error - mL	Prevalence	Error- mL
Post-Systolic Shortening	1/28 (3.6%)	8.0	6/32 (18.9 %)	3.7 ± 4.5
AVC within 1 Phase of the Minimum Global Volume	25/28 (89.3%)	0.8 ± 1.1	25/32 (78.1%)	0.4 ± 0.7
Late Aortic Valve Closure	2/28 (7.1%)	1.9 ± 1.4	1/32 (3.1%)	1.0

Underestimation of SV and EF due to different ED and ES phase selection methods relative to global volume maximum and minimum Values.

Underestimation of SV and EF due to different ED and ES phase selection methods relative to global volume maximum and minimum Values.