Torsional Adaptations in the Left Ventricle Post-Myocardial Infarction

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Abstract

Myocardial infarction (MI) induces cardiomyocyte death and scar formation, triggering functional adaptations of the left ventricle (LV). The quantification of cardiac contractile function via regional indices, such as cardiac strains and torsion, has shown the potential to provide a mechanistic link between LV structure and function. Indeed, torsion is an integral component of LV contractility resulting from the complex helical arrangement of myofibers within the LV microstructure. We hypothesize that region-specific LV torsion can be used to assess MI-associated impaired contractility and provide added prognostic value to functional indices such as ejection fraction (LVEF). A longitudinal study evaluated LV torsion in a rodent model of MI at 2 weeks (2-WK) and 4 weeks post-MI (4-WK). Speckle-tracking echocardiography was used to calculate regional cardiac rotations at basal, mid, and apical slices. Torsion was subsequently evaluated as the two-dimensional shear angle at all slices relative to basal and mid slices. Whereas the reduction in LVEF was insignificant at 2-WK post-MI, a significant drop in torsion was evident in 2-WK and statistically maintained in 4-WK post-MI. While reduced LVEF is a crucial indicator of LV systolic dysfunction, assessing LV regional kinematic alterations through cardiac torsion can provide insights into the pathophysiological link between tissue-level LV myocardial remodeling and functional adaptations in MI.

1. Introduction

Myocardial infarction (MI) is associated with cardiomyocyte death and the subsequent formation of a non-contractile fibrotic scar in the left ventricle (LV). Acute MI is followed by a series of cardiac remodeling events to compensate for (i) the regional impairments in LV contractility and (ii) the stiffening of the LV scar tissue [1, 2]. This series of remodeling events can lead to further decompensation of the LV and ultimately result in the transition of the LV to heart failure. Standard diagnosis includes the assessment of global cardiac performance through the evaluation of the ejection fraction (LVEF), stroke volume (SV), and end-diastolic volume (EDV) [3]. Despite the benefits of these functional indices, they remain global measures of LV contractility that provide confounded and low sensitivity to tissue-level remodeling events [4]. For instance, remodeling may manifest as altered anisotropy in the arrangement of myofibers, thus compromising LV regional contractile function without significant changes in the global measures of the LV function. Indeed, the myocardium is composed of a complex transmural helical fiber structure, with both myofiber contraction and helicity leading to the twisting of the LV, i.e., LV torsion. The resulting counter-rotation of the LV apex with respect to the base is considered a significant contributor to the proper contractile function of the LV [5, 6]. We hypothesize that region-specific LV torsion estimated using brightness-mode (B-mode) echocardiography can provide added prognostic value to functional indices in the evaluation of MI due to their direct mechanistic link with tissue-level remodeling.

The rising prevalence of B-mode echocardiography in estimating structural indices such as strains and torsion has provided significant mechanistic insights into the progression of cardiovascular diseases [7]. However, the association between deteriorating cardiac function due to MI and LV torsion remains largely understudied. Moreover, the common practice of reporting structural indices as a single global representative measure of cardiac contractility limits the detection of regional variations in cardiac remodeling. Indeed, the myocardium experiences large deformations resulting in complex contractile patterns, necessitating a thorough investigation of region-specific variations in torsion. Accordingly, a longitudinal study was implemented to investigate the time-course progression of LV torsion in a rodent model of MI. Short-axis (SA) B-mode echocardiography was performed at the base, mid,

and apical sections of the LV in Wistar-Kyoto rats, and a speckle-tracking algorithm was implemented to assess myocardial torsion through calculating the in-plane rotation of the speckles.

2. Methods

2.1. Rodent Model of MI

A total of nine male Wistar-Kyoto rats, 8 weeks old at the start of the experiment, were used in this study. Anteriobasal infarct was induced in six rats by ligation of the left anterior descending artery near the base of the heart. Animals were sacrificed at 2-week (n=3) and 4-week (n=3) post-MI timepoints (hereafter referred to as 2-WK and 4-WK, respectively). Three animals were used as control subjects and were sacrificed 1 week after receiving sham surgery. All animals used in this work were treated in accordance with guidelines approved by the Institutional Animal Care and Use Committee (IACUC) at the Texas Heart Institute, and all procedures were performed following protocols approved by the Texas Heart Institute's IACUC.

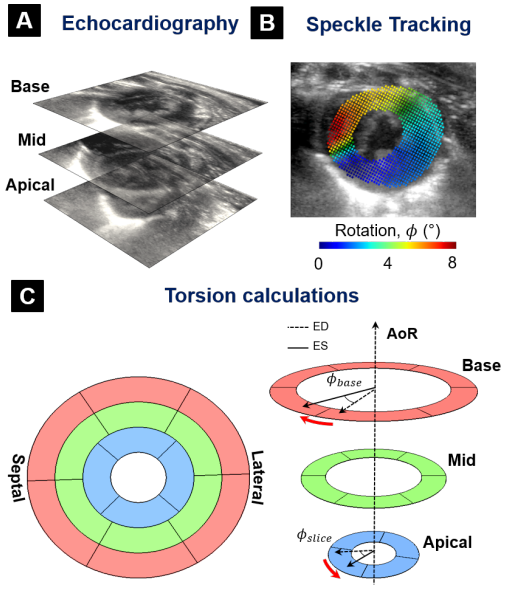

Figure 1: (A) Representative short-axis (SA) parasternal brightness-mode (B-mode) echocardiography at the base, mid, and apical sections of the left ventricle (LV) in a control rat. (B) Representative speckle-tracking derived rotations (ϕ) at the mid-section at end-systole (ES) relative to end-diastole (ED). (C) Schematic outlining the torsion calculations between the base (red) and apical (blue) sections of the LV using speckle-tracking-derived ϕ at the base and apex. AoR: axis of rotation.

2.2. Echocardiography

B-mode echocardiography was performed to quantify the structure and function of in-vivo rat hearts using the FUJIFILM/Visualsonic Vevo 3100 system with an MX550D probe (center transmit frequency of 20 MHz). Rats were anesthetized with inhaled isoflurane with pure oxygen carrier at light sedation (0.5-1%). Electrocardiograms (ECGs) and respiration were continuously monitored. Stage heating and heat lamps were used to keep rats warm. Specific measurements included chamber dimensions and ejection fractino from parasternal long-axis views and twist from short-axis (SA) views (Fig. 1A).

2.3. Speckle-tracking

A speckle-tracking framework was implemented to evaluate cardiac torsion at end-systole (ES) with respect to end-diastole (ED) [8]. A normalized cross-correlation algorithm was used to track pixel movement between two consecutive interrogation windows, $\mathbf{w}_1$ and $\mathbf{w}_2$ in the k^{th} Fourier space and the inverse Fourier transform was applied to derive the Cartesian displacements as:

$$\mathbf{u} = \text{argmax}\left\{\mathcal{F}^{-1}\left(\frac{\mathbf{W_1^k} \odot \overline{\mathbf{W_2^k}}}{|\mathbf{W_1^k} \odot \overline{\mathbf{W_2^k}}|}\right)\right\}, \qquad (1)$$

where $\mathbf{u}$ is the Cartesian displacement vector, $\mathcal{F}^{-1}$ denotes the inverse Fourier transform, $\odot$ denotes element-wise multiplication, the overline denotes the complex conjugate, and $\mathbf{W}_1$ and $\overline{\mathbf{W}}_2$ are the Fourier transforms of $\mathbf{w}_1$ and $\overline{\mathbf{w}}_2$, respectively. Thus, $\mathbf{u}$ was determined as the location of the peak normalized-cross correlation between $\mathbf{w_1}$ and $\mathbf{w_2}$. The Cartesian displacements, in conjunction with the dimensions of the LV, were then used to derive the cardiac rotations as described below.

2.4. Torsion calculation

The Cartesian displacement vector calculations were converted to the polar space (i.e., radius and azimuth) to quantify LV torsion in terms of rotations relative to a reference section that can be cast into an in-plane (two-dimensional) shear angle, denoted by $\mathrm{T}_{2\mathrm{D}}$ [9] (Figs. 1B, C). The center of mass was determined from the reconstructed LV geometry, and a longitudinal line passing through the base, the center of mass, and the apex at ED, was chosen as the axis of rotation (AoR). With the AoR as a reference, pixel-level in-plane rotations were derived from the corresponding position vectors at ED and ES (denoted by $\mathbf{R}_{\mathrm{ED}}$ and $\mathbf{R}_{\mathrm{ES}}$) as:

$$\phi = \tan^{-1}\left(\frac{|\mathbf{R}_{\mathrm{ED}} \times \mathbf{R}_{\mathrm{ES}}|}{\mathbf{R}_{\mathrm{ED}} \cdot \mathbf{R}_{\mathrm{ES}}}\right), \qquad (2)$$

where ϕ_{slice} and ϕ_{base} are the mean rotations at the section (slice) of interest and the base, respectively. Using the 2D rotations, $\mathrm{T}_{2\mathrm{D}}$ was defined as:

$$\mathrm{T_{2D}} = \frac{\phi_{\mathrm{slice}}\,\rho_{\mathrm{slice}} - \phi_{\mathrm{base}}\,\rho_{\mathrm{base}}}{\mathrm{D}}; \mathrm{T_{2D}} \in \left[-\frac{\pi}{2}, \frac{\pi}{2}\right], \quad (3)$$

where ρ_{slice} and ρ_{base} are the average epicardial radii about the AoR, and D is the distance between the base and the slice of interest, all at ES. Region-specific torsions were then measured as the peak $\mathrm{T_{2D}}$ between the (i) base and mid, (ii) mid and apical, and (iii) base and apical sections of the LV. Regional peak torsion was delineated by mapping values to a standard AHA 17 segment map. Significance was evaluated using unpaired one-way ANOVA analysis with all rats at 2- and 4-WK post-MI compared to the rats at baseline (CTL).

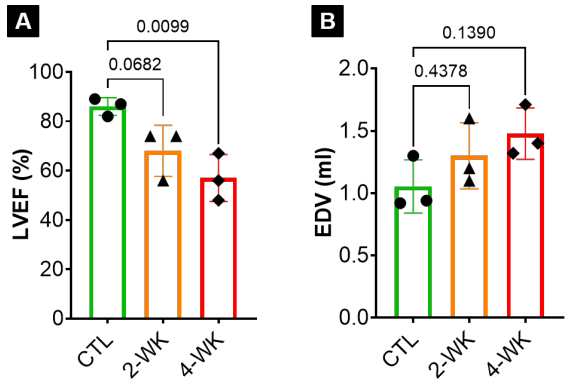

Figure 2: Organ-level functional indices, namely, (A) left ventricular ejection fraction (LVEF) and (B) end-diastolic volume (EDV) for rats at baseline (CTL, n = 3), two- and four-weeks-post myocardial infarction (2-WK and 4-WK; n = 3 each).

3. Results

Organ-level metrics indicated no significant change in the LVEF and EDV at 2-WK post-MI, with statistically significant deviations observed in LVEF at 4-WK post-MI, indicating a deteriorated cardiac function at the late stage of MI (Fig. 2). In contrast to the observed changes in functional indices, speckle-tracking revealed rapid deterioration in the rotation of the LV at the 2-WK terminal point, with reduced rotations obtained primarily at the apex (relative to the base) and base (relative to the mid) sections of the LV (Figs. 3A and B). Torsion calculations confirmed significant drops at both the 2-WK and 4-WK terminal points. Mid-section peak torsion (relative to the base) was significantly impaired at both 2-WK an 4-WK timepoints (Fig. 4A). The peak torsion calculated at the apex (relative to the base) was significantly reduced at 2-WK (Fig. 4B); in contrast, there was no significant change in the apex torsion with respect to the mid-section post-MI (Fig. 4C). The region-specific torsion markers provided greater statistical confidence than LVEF in detecting the time-course impairment of LV contractility. Specifically, basal-mid torsion was observed to be the most sensitive to MI (Fig. 4A), with a near 60% reduction in basal-mid torsion observed at 2-Wk post-MI (TL vs. 2-WK: 7.2781 $\pm$ 1.5685 vs. 2.8213 $\pm$ 0.5331) and a 80% reduction observed at 4-WK (CTL vs. 4-WK: 7.2781 $\pm$ 1.5685 vs. 1.0261 $\pm$ 0.3811).

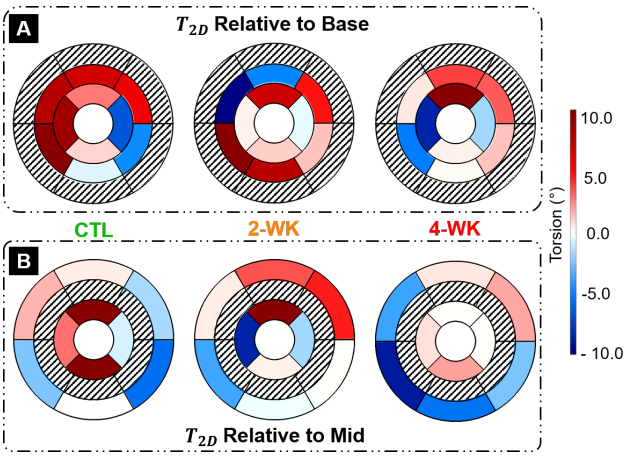

Figure 3: Representative distribution of torsion (T_{2D}) calculations obtained at (A) mid and apical sections relative to the base, and (B) base and apical sections relative to the mid. Rotations are visualized in an AHA 17 segment map at baseline (CTL), two- and four-weeks (2-WK and 4-WK) -post myocardial infarction. The outermost circle corresponds to the base, and the innermost corresponds to the apical section of the left ventricle. The hatched region denotes the reference section.

4. Discussion

While the reduction in (global) cardiac functional indices (LVEF and EDV) was observed to deteriorate with the time-course progression of MI, the evaluation of torsional characteristics of the LV yielded superior statistical significance. Additionally, region-specific torsional calculation revealed alterations in the torsional behavior of the LV at various sections across the presented longitudinal timepoints, highlighting the manifestation of MI-associated regional remodeling (Figs. 3 and 4). These observations suggest that the torsion shear angle offers detectable sensitivity to localized non-contractile scars and architectural changes in the LV. The association between reduced cardiac strains and localized scar formation has been established in previous studies [2, 10, 11], with structural indices providing greater sensitivity than traditional functional indices. Such contributors to LV contractile function are overlooked in gross organ-level volumetric assessments and general strain analysis. For instance, our findings suggest a more significant reduction of torsion at the apical than at the mid sections (relative to the respective control) at 2-WK post-MI, indicating region-specific alterations in torsion behavior due to MI (Fig. 3).
However, time-dependent torsion analysis at the apical section relative to the mid indicated no significant alterations post-MI. Additionally, in the control group, the peak

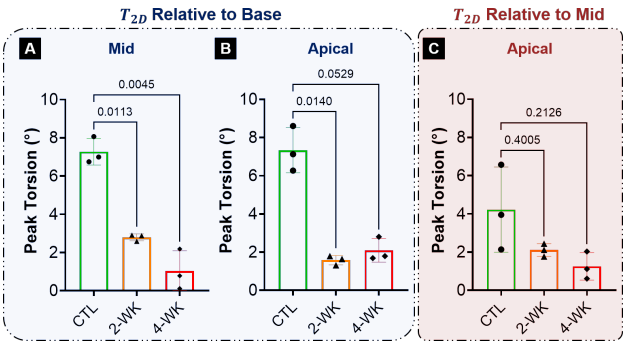

Figure 4: Time-course progression of region-specific torsion (T_{2D}) calculations for all rats at baseline (CTL; n = 3), two- and four-weeks-post myocardial infarction (2-WK and 4-WK; n = 3 each). Torsion was estimated as the average shear angle (Eq. 3) at (A) mid and apical sections, and (B) apical section relative to the base and mid sections of the left ventricle, respectively

torsion resulting from the counter-rotation of the apical section relative to the mid was ∼50% lower than that of the mid-section relative to the base, indicating a strong spatial torsion regionality even in a healthy heart. While torsional analysis may potentially improve the characterization of regional adaptations due to MI, none of the region-specific torsion metrics showed high levels of statistically significant confidence, i.e., $p < 0.001$, suggesting the necessity of larger sample sizes and further ex-vivo investigations comprising mechanical testing and histological examinations to correlate strains and torsion with fiber architecture and scar maturation [12]. While further investigations are required to confirm the link between scar formation and deteriorating LV torsion, our findings emphasize the importance of accurately quantifying such regionality in LV torsion. In conclusion, while reduced LVEF is a crucial indicator of LV systolic dysfunction, assessing regional kinematic changes such as torsion may provide mechanistic insights into LV remodeling and add prognostic value to global indices of LV function in MI.

Acknowledgments

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