**Torsional Mechanics of the Left Ventricle in Patients After Surgical Repair of Tetralogy of Fallot**

Yiu-fai Cheung; Sophia J Wong; Xue-cun Liang; Eddie WY Cheung

**Background:** This study aimed to test the hypothesis that alteration of left ventricular (LV) torsional mechanics occurs in patients after repair of tetralogy of Fallot (TOF) and is associated with right ventricular (RV) volume overload and changes in LV configuration.

**Methods and Results:** Fifty-five TOF patients aged 19.0±8.1 years and 27 age-matched healthy controls were studied. The LV and RV volumes were measured using 3-dimensional echocardiography while LV geometry was quantified by the diastolic eccentricity index (EI). The LV peak systolic torsion and systolic twisting and diastolic untwisting velocities were determined by speckle tracking. Compared with controls, patients had significantly greater RV end-systolic (P<0.001) and diastolic (P<0.001) volumes and LV diastolic EI (P<0.001). In contrast, LV peak apical rotation (P<0.001), systolic torsion (P=0.004), systolic twisting velocity (P=0.001), and diastolic untwisting velocity (P=0.001) were lower in patients than in controls. For the whole cohort, RV EDV and LV diastolic EI were negatively related to systolic torsion, systolic twisting velocity, and diastolic untwisting velocity (all P<0.001). Systolic torsion correlated strongly with diastolic untwisting velocity (r=0.72, P<0.001), while systolic twisting velocity correlated with LV ejection fraction (r=0.3, P=0.005).

**Conclusions:** LV torsional mechanics is impaired and is negatively related to RV volume overload and LV eccentricity in patients after TOF repair. (Circ J 2011; 75: 1735–1741)

**Key Words:** Speckle tracking echocardiography; Tetralogy of Fallot; Ventricular torsion

While right ventricular (RV) dysfunction has been the main concern in patients after repair of tetralogy of Fallot (TOF),1−3 the importance of left ventricular (LV) dysfunction as a risk factor of long-term adverse outcomes is increasingly acknowledged.4,5 Dysfunction of the left ventricle is characterized by reduced ejection fraction,4,6 altered systolic myocardial deformation,5,7 and systolic mechanical dyssynchrony.5,8 These LV functional abnormalities have been attributed to suboptimal ventricular-ventricular interaction,4,6 although the nature of this interaction remains to be defined.

Assessment of cardiac mechanics has extended from evaluation of linear to torsional deformation, which might provide new mechanistic insights. Twisting motion of the left ventricle during the ejection phase is important in the Frank–Starling mechanism,9 while untwisting contributes to LV diastolic relaxation and early diastolic filling.10 Interaction between LV subendocardial and subepicardial helical myocardial fibres has been proposed to explain the phenomenon of torsional deformation.11 Alteration of septal geometry and changes in LV shape due to volume overloading of the right ventricle might potentially distort this interaction and impair torsional deformation. In the present study, we tested the hypothesis that alteration of LV torsional mechanics occurs in postoperative TOF patients and is associated with RV volume overload and changes in LV configuration.

**Methods**

**Subjects**

Fifty-five patients who had undergone surgical repair of TOF with transannular patch enlargement of the RV outflow were recruited consecutively from the cardiac clinic of Queen Mary Hospital. From the case records, the following data were retrieved: age at operation, types of surgical procedure, and duration of follow up since total repair. Twenty-seven healthy subjects, including those followed up for non-specific chest pain and palpitation but without documented cardiac arrhythmias and healthy siblings, were recruited as controls. The weight and height of all subjects were measured and the body surface area was calculated accordingly. The Institutional Review Board approved the study and all of the subjects gave...
informed consent.

2- and 3-Dimensional Echocardiography

Transthoracic echocardiography was performed using the Vivid 7 ultrasound system (General Electric, Vingmed, Horten, Norway). Measurements were made in 3 cardiac cycles, and the average was used for statistical analyses. The echocardiographic recordings were stored in a digital versatile disc for offline analyses using EchoPAC software (General Electric, Vingmed, Horten, Norway).

Eccentricity of the left ventricle was determined from 2-dimensional images acquired from the parasternal short-axis view. The maximum distance from the endocardial surface of the mid-ventricular septum to that of the posterolateral LV free wall (D1), and the distance of the orthogonal axis between the endocardial surfaces of the anterior and inferior LV free walls (D2) were measured at end-diastole. The LV diastolic eccentricity index (EI) was calculated as D2/D1. The greater the EI, the more compressed the left ventricle is.

Real-time 3-dimensional echocardiographic imaging was performed from the apical view using a matrix-array transducer. The LV and RV 3-dimensional data sets were acquired separately so as to include the entire ventricular chamber in

Figure 1. Profiles of (A) torsion (white) derived from the difference between apical rotation (blue) and basal rotation (purple), and (B) twisting and untwisting velocities of the left ventricle.
Full-volume acquisition was performed during breathhold to minimize translation artifact between the 4 subvolumes. Offline analyses of 3-dimensional data sets were performed using commercial 4D LV and RV analysis software (Tomtec Imaging Systems, Unterschleisheim, Germany).

Determination of LV and RV volumes and reproducibility of measurements have been reported previously. Briefly, LV quantitative analysis involved tracing of the endocardial border in 3 planes (2-, 3- and 4-chamber planes) at the end-systole and end-diastole. A LV cast was then created for derivation of LV end-diastolic and end-systolic volumes. For quantitative RV analysis, endocardial borders of the right ventricle in 3 orthogonal planes (sagittal, coronal, and 4-chamber planes) were traced semi-automatically at the end-diastole and end-systole. Trabeculations were included in the endocardial rim. An RV cast was then created for derivation of RV end-diastolic and end-systolic volumes.

LV Torsion
LV torsion was assessed by the speckle tracking echocardiographic technique. The apical and basal short-axis planes of the left ventricle were acquired using the B-mode. The basal level was defined as the level of the mitral valve, while the apical level was defined as that of the LV cavity alone with no visible papillary muscles. The endocardium at each of the 2 levels was traced and a speckle-tracking region of interest was then generated automatically to include the myocardium. Rotation of the basal and apical planes was determined. The apical and basal acquisitions selected for calculation of torsional parameters were carefully matched for similar RR intervals. Torsion was calculated as the apex-to-base difference in rotation, while systolic twisting velocity was defined by the positive rate of torsional deformation during the ejection phase and diastolic untwisting velocity by the negative rate of torsional deformation during early diastole. The following LV torsional indices were obtained: peak LV torsion, time to peak LV torsion from the onset of the QRS, peak systolic twisting velocity, and peak diastolic untwisting velocity. Figure 1 shows examples of a torsion curve and a torsional velocity profile.

RV, right ventricular; EDV, end-diastolic volume; ESV, end-systolic volume; LV, left ventricular.

*Statistically significant.

Table. 3-Dimensional Echocardiographic and Torsional Parameters of Patients and Controls

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=55)</th>
<th>Controls (n=27)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td><strong>Echocardiographic parameters</strong></td>
<td></td>
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<tr>
<td>Indexed RV EDV (ml/m²)</td>
<td>77±25</td>
<td>45±21</td>
<td>&lt;0.001*</td>
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<tr>
<td>Indexed RV ESV (ml/m²)</td>
<td>40±18</td>
<td>19±6</td>
<td>&lt;0.001*</td>
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<tr>
<td>RV ejection fraction (%)</td>
<td>50±7</td>
<td>57±5</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Indexed LV EDV (ml/m²)</td>
<td>48±11</td>
<td>46±8</td>
<td>0.42</td>
</tr>
<tr>
<td>Indexed LV ESV (ml/m²)</td>
<td>20±6</td>
<td>17±4</td>
<td>0.005*</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>58±6</td>
<td>63±5</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Torsional parameters</strong></td>
<td></td>
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<tr>
<td>Basal rotation (degree)</td>
<td>–3.3±2.3</td>
<td>–3.9±2.1</td>
<td>0.28</td>
</tr>
<tr>
<td>Apical rotation (degree)</td>
<td>6.9±3.3</td>
<td>10.1±3.8</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Peak systolic torsion (degree)</td>
<td>8.6±4.8</td>
<td>12.1±4.8</td>
<td>0.004*</td>
</tr>
<tr>
<td>Time to peak LV torsion (ms)</td>
<td>470±98</td>
<td>479±63</td>
<td>0.59</td>
</tr>
<tr>
<td>Peak systolic twisting velocity (degree/s)</td>
<td>65.4±21.8</td>
<td>87.9±29.1</td>
<td>0.001*</td>
</tr>
<tr>
<td>Peak diastolic untwisting velocity (degree/s)</td>
<td>78.9±31.1</td>
<td>106.6±35.9</td>
<td>0.001*</td>
</tr>
<tr>
<td>RR interval (ms)</td>
<td>857±132</td>
<td>837±136</td>
<td>0.52</td>
</tr>
</tbody>
</table>

RV, right ventricular; EDV, end-diastolic volume; ESV, end-systolic volume; LV, left ventricular.

Statistical Analysis
All of the variables are presented as mean±SD. The RV and LV volumes were indexed to body surface area. Differences in demographic and echocardiographic variables between patients and controls were compared using unpaired Student’s t-test and Fisher’s exact test where appropriate. Pearson correlation analysis was used to assess for relationships between LV torsional indices, LV EI, and RV end-diastolic volume. Multiple linear regression analysis was used to determine significant correlates of peak LV torsion, and peak twisting and untwisting velocities. Logarithmically transformed absolute torsion and torsional velocities were used in univariate and multivariate correlation analyses. A P value ≤0.05 is considered statistically significant. All statistical analyses were performed using SPSS version 11.5 (SPSS Inc, Chicago, Illinois, USA).
Results

Subjects
Fifty-five patients (32 males), aged 19.0±8.1 years, who had undergone surgical correction of TOF at age of 2.4±2.3 years were recruited. The patients were studied at 16.6±7.0 years after surgery and were symptom-free at the time of study. The 27 controls (12 males) were studied at an age of 17.2±6.2 years (P=0.25). Compared with controls, patients tended to have a smaller body mass index (18.6±3.5 kg/m² vs. 20.5±4.0 kg/m², P=0.058) but had a similar body surface area (1.4±0.4 m² vs. 1.5±0.3 m², P=0.14).

2- and 3-Dimensional Echocardiographic Findings
Compared with the controls, patients had significantly larger indexed RV end-diastolic volume (P<0.001), RV end-systolic volume (P<0.001), and LV end-systolic volume (P=0.005), and lower RV (P<0.001) and LV ejection fraction (P<0.001) (Table). In contrast, the indexed LV end-diastolic volume was similar between patients and controls (P=0.42).

The LV diastolic EI was significantly greater in patients than controls (1.3±0.2 vs. 1.0±0.2, P<0.001), suggesting greater distortion of the septal geometry and compression of the left ventricle. The LV diastolic EI correlated significantly with indexed RV end-diastolic volume (r=–0.70, P<0.001) (Figure 2).

LV Torsional Parameters
The LV torsional parameters in patients and controls are summarized in Table. Compared with controls, patients had significantly reduced LV apical rotation (P<0.001), peak systolic torsion (P=0.004), peak systolic twisting velocity (P=0.001), and peak diastolic untwisting velocity (P=0.001). In contrast, the basal rotation (P=0.28) and the time to peak LV torsion from the onset of the QRS (P=0.59) were similar between patients and controls.

The magnitude of rotation of the 6 apical segments in patients and controls is shown in Figure 3. Compared with controls, patients had a significantly reduced regional rotation of all the apical segments (all P<0.05).

For the whole cohort, RV EDV and LV diastolic EI correlated negatively with peak systolic torsion (r=0.48, P<0.001 and r=–0.42, P<0.001, respectively), systolic twisting velocity (r=–0.51, P<0.001 and r=–0.36, P=0.001, respectively), and diastolic untwisting velocity (r=–0.53, P<0.001 and r=–0.37, P=0.001) (Figure 4). The magnitude of peak systolic torsion correlated strongly with diastolic untwisting velocity (r=0.72, P<0.001). An impact of reduced LV systolic twisting on global LV systolic function was reflected by the positive correlation of peak systolic twisting velocity with LV ejection fraction (r=0.3, P=0.005).

Multiple linear regression analysis of the entire cohort identified indexed RV end-diastolic volume (β=–0.41, P=0.001), body mass index (β=–0.23, P=0.022), and the status being patient vs. control (β=–0.25, P=0.038) as significant determinants of LV systolic torsion after adjustment for age, sex, and LV diastolic EI. Significant determinants of LV systolic twisting velocity were indexed RV end-diastolic volume (β=–0.37, P=0.002) and patient status (β=–0.28, P=0.019), while that of LV diastolic untwisting was indexed RV end-diastolic volume (β=–0.53, P<0.001). For patients, the age at operation or duration of follow up did not correlate with any of the torsional parameters (all P>0.05).

Discussion
The present study provides evidence of impaired systolic and diastolic torsional deformation of the left ventricle in patients after TOF repair. Important findings in patients are reduced LV torsion, systolic twisting velocity, and diastolic untwisting velocity. The observed reduction of LV torsion in patients is primarily related to a decrease in systolic rotation of the LV apex. Furthermore, RV volume overload and greater LV eccentricity were found to correlate negatively with systolic and diastolic parameters of torsional deformation.

The understanding of torsional mechanics in congenital
LV Torsion in Repaired TOF

heart disease is extremely limited. In patients who have undergone Senning operation for complete transposition of the great arteries, Pettersen et al have demonstrated the absence of systemic RV torsion, which might have implications on energy-inefficient ejection and progressive myocardial dysfunction. In patients with functionally single ventricles having a RV morphology, abnormal systemic RV torsion has similarly been reported.

Alteration of LV mechanics in postoperative TOF patients is increasingly recognized. Using tissue Doppler or speckle tracking echocardiography, we and others have reported on the reduction of LV systolic strain in the longitudinal, circumferential, and radial dimensions. In particular, circumferential myocardial deformation has been found to be a significant correlate of RV volume and an independent predictor of peak oxygen consumption during treadmill exercise testing. Additionally, dysynchrony of LV contraction has also been shown to be associated with the severity of RV volume overload in these patients and have implications on global LV systolic function. Distortion of septal geometry secondary to RV volume overload has been hypothesized as a possible mechanism that underlies suboptimal ventricular–ventricular interaction. These previous studies have nonetheless focused on the abnormalities of linear deformation of the LV myocardium. Recently, van der Hulst et al have reported the reduction of LV systolic apical rotation and torsion in patients after repair of TOF. The present study further demonstrates the impairment of the rate of systolic twisting and diastolic untwisting of the left ventricle, and their associations with RV volume overload and LV configuration.

The underlying mechanisms of abnormal LV torsional mechanics in these patients are probably multifactorial. Our finding of association between greater LV eccentricity and worse torsional mechanics suggests that alteration of LV configuration might play an important pathogenic role. A framework of dynamic interaction between subepicardial and subendocardial helical fibres has been proposed to explain LV twisting and untwisting motions. Theoretical modeling further suggests a relationship between the magnitude of LV torsion and angulation of the myocardial helical fibres.
patients with dilated cardiomyopathy, a linear relationship between LV sphericity, a ratio of long-axis to short-axis dimension, and LV torsion has been described. Interestingly, in the same study, a parabolic relationship between these parameters was found in healthy subjects, suggesting that either decreased or increased angle of fibre orientation might be detrimental to LV torsional mechanics. The changes in subepicardial and subendocardial fibre orientation in our patients secondary to RV dilation might perhaps explain the observed differences in torsional mechanics compared with controls, although this remains speculative. Interestingly, an inverse relationship between LV end-diastolic EI and LV torsion has similarly been reported recently in adult patients with pulmonary hypertension.

The predominant effect of RV dilation and LV compression on apical rotation, and hence LV torsion, is intriguing. While the exact mechanism remains to be elucidated, the recent report of differential response of the three RV components to volume overload in the setting of TOF might shed some light on a possible explanation. In the aforementioned study, the RV apical component, as a contrast to the inlet and outlet components, has been shown to take up the greatest part of the volume load secondary to pulmonary regurgitation while providing the major ejectile momentum of the ventricle. Disproportional enlargement of the RV apical trabecular component might potentially exert more prominent effects on LV apical rotation because of the ventricular–ventricular interaction. Indeed, apical RV strain has been shown recently to correlate with apical LV rotation. In contrast, volume overloading of the right ventricle in adults with secundum atrial septal defect has been shown to be associated with reduced LV torsion, due primarily to impaired basal rotation.

Loading conditions and abnormal myocardial deformation might possibly also influence LV torsional mechanics. Although ventricular afterload was not determined in the present study, we and others have previously demonstrated stiffening of the central arteries, increased augmentation of central aortic pressure, and elevated characteristic impedance of the systemic arterial tree, all of which can increase LV afterload and potentially exert negative effects on torsion and diastolic untwisting of the left ventricle. Additionally, dyssynchronous contraction of the left ventricle in subjects with acute RV apical pacing and in those with advanced heart failure and prolonged QRS duration has been reported to be associated with a significant reduction in LV torsion. The documented mechanical LV dysynchrony in patients after TOF repair, might therefore also contribute to the observed reduction in systolic torsion.

The findings of the present study have several important clinical implications. Reduction of torsion increases endocardial stress and strain and hence oxygen demand, thereby reducing the efficiency of LV function. Additionally, impaired LV torsional mechanics might impact on global LV systolic function. Our findings of a positive correlation between LV systolic twisting velocity and LV ejection fraction concurs with those reported previously. Importantly, there is increasing evidence to suggest that LV torsion might be superior to LV ejection fraction in the characterization of abnormal haemodynamics in patients with heart failure. Furthermore, abnormal systolic LV torsion has been shown to be related to diastolic dysfunction. As shown in this and previous studies, the magnitude of LV systolic torsion is related inversely to the rate of untwisting during diastole. The storage of potential energy during systolic torsional deformation and its release as kinetic energy to facilitate diastolic filling is of particular relevance in postoperative TOF patients. In adults with isolated LV diastolic dysfunction, a progressive increase in pulmonary arterial pressure has been shown for each step-up in grading of diastolic dysfunction. Albeit speculative, as the extent of diastolic recoil is regarded as an important contributor of LV suction, a reduced rate of LV diastolic untwisting might potentially increase hydraulic impedance of the pulmonary vascular bed and hence augment the severity of pulmonary regurgitation.

Two limitations to this study warrant comments. First, the cross-sectional design of the study does not provide information on the time-course of alteration of torsional parameters after surgery and its prognostic implications. Second, imaging of apical and basal segments was performed sequentially rather than simultaneously, thus introducing a potential error in the generation of the torsion-time curve. To minimize the error, we have matched the RR intervals of the 2 segments before calculation of the torsional parameters. In conclusion, our findings provide evidence of altered systolic and diastolic LV torsional mechanics in patients after surgical repair of TOF, which is related negatively to RV volume overload and LV eccentricity.

References


