Kinetics of Left Ventricular Strains and Torsion During Incremental Exercise in Healthy Subjects: The Key Role of Torsional Mechanics for Systolic-Diastolic Coupling

Running title: LV Torsion During Incremental Exercise

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ABSTRACT

**Background** – Dynamics of systolic and diastolic strains and torsional mechanics of the left ventricle (LV) and their relation to diastolic filling have never been evaluated at various exercise intensities.

**Methods and Results** – Speckle tracking echocardiography (STE) was performed in 20 healthy sedentary subjects at rest and during a progressive submaximal exercise test at 20%, 30% and 40% of maximal aerobic power. LV twist increased progressively with exercise intensity (10.5±3.2 to 15.8±4.5 deg, $P<0.001$), whereas longitudinal strain remained unchanged after the first workload, underlining the key role of torsional “reserve” in systolic-diastolic-coupling during exercise. The increase in diastolic untwisting ($-88.7±34.2$ to $-182.9±53.5$ deg.s$^{-1}$, $P<0.01$) was correlated to enhanced systolic twist ($R=0.61$, $P<0.001$), and its magnitude of increase was significantly higher compared to diastolic longitudinal and circumferential strain rates ($119±64$ versus $65±44$ and $57±24$%, respectively), emphasizing its contribution to diastolic filling. The timing of peak untwisting and the chronology of diastolic mechanical events were unchanged during effort. Untwisting was driven mainly by apical rotation and determined mitral opening and isovolumic relaxation time ($R=0.47$ and 0.61 respectively, $P<0.001$), whereas basal rotation, longitudinal and circumferential diastolic strain rates were major determinants of increased early diastolic filling ($R=0.64$, 0.79 and 0.81 respectively, $P<0.001$).

**Conclusions** – The use of STE gives new insights into physiologic adaptive LV mechanics during incremental exercise in healthy subjects, underlining the key role of torsional mechanics. It might be useful to better understand the mechanisms of diastolic dysfunction and exercise intolerance in various pathologic conditions.

**Key Words:** speckle tracking echocardiography – exercise – left ventricular torsion - left ventricular untwisting
INTRODUCTION

During diastole, left ventricle (LV) filling results from a complex interplay between numerous factors such as myocardial relaxation, LV compliance, untwisting and loading conditions. During systole, contraction of the cardiomyocytes induces not only normal, but also shear strains, including LV torsion (i.e. basal clockwise rotation and apical counterclockwise rotation) due to the helical orientation of myofibers. LV diastolic untwisting is a consequence of both an active relaxation of the myocardium and a release of the energy stored in compressed titin and elastic components of the interstitium. Importantly, untwisting occurs predominantly during isovolumic relaxation (IVR) and promotes LV “suction” by increasing LV intraventricular (i.e. from apex to base) pressure gradients. Interestingly, LV untwisting is decreased and/or delayed in states associated with diastolic dysfunction such as tachycardia-induced heart failure, dilated cardiomyopathy, aortic stenosis, or following strenuous exercise. The evaluation of LV normal and shear strains and their timing during diastole is therefore of significant interest to assess diastolic dysfunction.

Exercise stress echocardiography is a powerful tool to provide additional diagnostic and prognostic information in a variety of diseases and allows early detection of subtle myocardial dysfunction. During exercise, the increase in stroke volume is limited by diastolic filling, as the increase in heart rate shortens the duration of diastole. Additionally, left ventricular filling must be accomplished at relatively low filling pressures to avoid pulmonary vascular congestion. Early studies underlined the key role of untwisting in LV filling during exercise, but the time course of diastolic mechanical events, including both LV strains and torsional mechanics, has not been fully described. Moreover, no data are available...
regarding kinetics with increasing exercise intensity and timing of diastolic myocardial events during an incremental exercise. Recently, speckle tracking echocardiography (STE) provides the ability to quantify LV strains \(^{18}\) and torsion \(^{19}\) at rest and during exercise \(^{15,16}\).

In the present study, we aimed to describe dynamics and timing of LV myocardial mechanical events during an incremental exercise test. We used STE at rest and during an exercise conducted on a dedicated ergometer. We hypothesized that (1) diastolic untwisting would increase progressively with exercise intensity paralleling enhanced systolic twisting (2) amplitude and timing of LV diastolic mechanics would adapt to preserve or enhance LV filling when diastole shortens during effort.

**METHODS**

**Study population**

We evaluated 20 young, healthy and sedentary adult males (mean age: 25 ± 9 yr old). None of them reported regular training habits nor had any clinical or anamnestic evidence of cardiovascular disease or arterial hypertension. Subjects were excluded if resting echocardiography demonstrated ejection fraction < 50%, significant valvular disease, abnormal right ventricle function, or systolic arterial pulmonary pressure > 35 mmHg. This study received approval from the local ethics committee and written informed consent was obtained from all subjects.

**Experimental protocol**
Body height and mass were assessed. The maximal aerobic power was initially estimated via the Wasserman equation for the subject’s age and body mass, and corrected for the semi-supine position (20% was removed from normal values).

The subjects were installed on a dedicated semi-supine cycling ergometer (E-Bike ergometer, GE Healthcare, Horten, Norway). After a 15 to 20 minutes resting period, each subject underwent an exercise test including 3 stages of 6 minutes duration at 20%, 30% and 40% of their maximal aerobic power (respectively labeled W1, W2, and W3), and then stages of 1 minute from 50% to exhaustion by 10% increments. The pedaling rate was kept constant at 70 rpm for all subjects.

Two-dimensional (2-D) and Doppler Echocardiographic data were recorded at the end of the resting period and during the last 4 minutes of W1, W2, and W3 stages. During the last 30 seconds of the test we measured stroke volume. Gas exchanges were measured continuously by means of a cardiopulmonary exercise system (Ergocard, Medisoft S.A, Sorinnes, Belgium). Systemic arterial blood pressure was measured during each stage of exercise in the left arm using manual sphygmomanometry and auscultation. Mean arterial pressure was calculated as $1/3 \times$ systolic pressure $+ 2/3 \times$ diastolic pressure.

**Echocardiographic data acquisition**

Images were obtained using a commercially available system (Vivid 7, GE Healthcare, Horten, Norway) with a 3.5 Mhz sector scanning electronic transducer. We recorded cine loops in parasternal short axis (basal, papillary muscle and apical levels) and in apical 4-chambers views. Two-dimensional grayscale harmonic images were obtained at a rate of 65 to 90 frames per second, and color tissue velocity images were acquired at a rate of 120 to 140 frames per second. Images were acquired in cine loops triggered to the QRS complex and
saved digitally for subsequent off-line analysis with dedicated software (EchoPac 6.0, GE Healthcare, Horten, Norway).

2-D and Tissue Doppler echocardiography

M-Mode measurements were obtained off-line from the parasternal short-axis view recorded at the papillary muscle level. Pulsed Doppler LV inflow (E and/or A waves) recordings were performed in the apical 4-chamber view. Aortic blood flow velocity was recorded in the ascending aorta with a 2.0 Mhz transducer (Pedof) placed at the suprasternal notch to assessed stroke volume and cardiac output, as previously used in our laboratory 20, 21. Systemic vascular resistance was estimated at each workload as mean arterial pressure divided by cardiac output. We measured the time delay in milliseconds from the onset of the ECG QRS interval to the onset of aortic blood flow (aortic opening, AO), the peak of aortic blood flow (Peak-S), the end of aortic blood flow (aortic closure, AC), the onset of early filling blood flow (mitral opening, MO), the peak of early filling blood flow (Peak-E) and the end of early filling blood flow (End-E). Isovolumic relaxation time (IVRT) was calculated as MO - AC.

Tissue Doppler evaluation was performed off-line from color cine loops recorded in the apical 4-chamber view. We assessed wall motion velocities at the mitral annulus level on the septal and lateral walls. The ratio transmitral peak-E on peak early myocardial velocity of the lateral wall was used as an index of LV filling pressure 22.

Speckle tracking echocardiography
Analysis of strain and torsion was conducted as previously described 11, 23. After manually tracing the endocardial border on the end-systolic frame of the 2D sequence, the software automatically tracked myocardial motion. Whenever the software signaled poor tracking efficiency, the observer readjusted the endocardial trace line and/or the region of interest width until a better tracking score could be obtained. Results were averaged on three to five cardiac cycles. LV longitudinal strain and strain rate (SR) were assessed using an apical 4-chamber view. Circumferential strain, SR and LV rotation and rotational rate were assessed from short-axis views at basal and apical levels. Care was taken to ensure that the basal short-axis plane contained the mitral valve, and that the apical plane was acquired with the probe in a caudal position to improve LV apical rotation measurement 24.

2D-Strain data were processed with a specific toolbox (Scilab 4.1, Consortium Scilab, INRIA-ENPC, Paris, France) developed in our laboratory. For temporal analysis, this software adjusted all strain variables for inter-subjects differences in heart rate and transducer frame rate acquisition. The time sequence was normalized to the percentage of systolic and diastolic duration (i.e. AC represented 100% of systole and end of cardiac cycle represented 100% of diastole) using interpolations. After normalization, the software averaged each data from 3 to 5 cardiac cycles and performed the detection of peak strains events and their timing (expressed in percentage of systolic duration). Net LV torsion was calculated as the instantaneous difference between LV apical - LV basal rotations. We calculated the following indexes of diastolic function during isovolumic relaxation (IVR): 1) untwisting angle (UT°,°) = twist at AC - twist at end-IVR; 2) percentage of untwisting during IVRT (%UTIVRT, %) = (UT° / twist at AC)*100; and 3) mean rate of untwisting during the IVRT (mean UTIVRT, °.s⁻¹) = -UT° / IVRT. To assess the dynamics of global LV torsion and its relation to radial displacement (reflecting volumetric changes of the LV) throughout the cardiac cycle, we constructed twist-radial displacement loops 11, 25. Radial displacement data from 6 segments in
basal and apical short axis planes were averaged to obtained the mean value of radial
displacement.

Statistical analysis

All values in the text and tables are expressed as mean ± SD and are shown as mean ±
SE in figures. The statistical analysis was performed using specific software (Statview 5.0,
SAS Insitute Inc. Cary, USA). For each cardiac variable, an analysis of variance with repeated
measures was performed with post hoc test using Bonferroni correction. Linear regressions
were performed to determine the relations between IVRT, peak-E, and LV diastolic
mechanical events. A multiple stepwise regression analysis was done to determine the
mechanical events responsible for the increase in early filling during effort. Statistical
significance for all analysis was assumed if P < 0.05. Intraobserver reproducibility of speckle
tracking evaluation was previously assessed in 12 subjects and was inferior at 8% for both
strains and rotations.

RESULTS

Height and body mass of the subjects were 177 ± 5 cm and 72 ± 8 kg, respectively.
Resting echocardiographic and blood pressure data are presented in table 1. At the end of
exercise, the maximal values were as follows: aerobic power: 221 ± 33 W, oxygen uptake: 34
± 5 mL.min⁻¹.kg⁻¹, heart rate: 179 ± 12 bpm, systolic and diastolic pressures: 197 ± 8 and 99 ±
7 mmHg, SV: 115.9 ± 17.3 mL and cardiac output: 20.6 ± 2.7 L.min⁻¹. The W1, W2, and W3
stages were performed at 19 ± 1, 28 ± 1 and 38 ± 2% of maximal aerobic power, respectively.
Heart rate during each stage was respectively 100 ± 12, 110 ± 12 and 121 ± 12 bpm.
Kinetics of LV hemodynamic parameters

Kinetics of LV internal diameters and SV are shown in figure 1. LV end-diastolic diameter increased from rest to W1, and then slightly decreased from W1 to W3. LV end-systolic diameter progressively decreased from rest to W3. Stroke volume increased by 14 ± 8 % from rest to W1 and then remained constant until W3. Peak-E increased from rest to W2 (0.88 ± 0.19 versus 1.23 ± 0.17 m.s⁻¹, P<0.0001) then remained constant (1.23 ± 0.17 versus 1.28 ± 0.17 m.s⁻¹, NS), whereas mean peak early diastolic myocardial velocity increased only between rest and W1 (12.4 ± 1.7 versus 14.6 ± 1.3 cm.s⁻¹, P<0.0001) then plateaued until W3 (14.6 ± 1.3 versus 14.7 ± 1.9 cm.s⁻¹, NS). LV filling pressure increased from rest to W1 (6.5 ± 1.1 versus 7.5 ± 1.4, P<0.0001), and then remained constant (7.5 ± 1.4 versus 8.1 ± 1.5, NS).

Kinetics of LV systolic strains

Kinetics of LV longitudinal and circumferential (averaged from basal and apical levels) peak systolic strains and LV rotations are shown in figure 2. LV longitudinal strain increased only from rest to W1, whereas LV circumferential strain and rotations progressively increased from rest to W3. As a result, LV torsion increased progressively from rest to W3 (10.5 ± 3.2 to 15.8 ± 4.5°, P<0.0001). Times to peak strains and torsion did not change during exercise excepted for LV apical rotations which appeared earlier at W2 and W3 (table 2).

Peak LV systolic SR and rotational and twisting rates progressively increased from rest to W3. Respective times to peak were not affected by exercise intensity except for LV peak basal rotational rate which was significantly delayed during exercise. LV peak apical...
rotational rate showed no significant change from rest to exercise, and occurred earlier than all other peak SR (table 3) independently of exercise intensity.

**Kinetics of LV diastolic strains**

During diastole, peak LV SR, rotational and untwisting rates increased progressively from rest to W3 (table 3). A strong correlation was observed between peak LV torsion and peak LV untwisting rate (R=0.61, *P*<0.001). The magnitude of increase (expressed in percentage compared to resting conditions) was significantly higher for LV untwisting rate (119 ± 64 %) than for changes of peak longitudinal and circumferential diastolic SR (65 ± 44 and 57 ± 24 %, respectively) (figure 3). Whatever the exercise intensity, peak LV apical rotational and untwisting rates occurred closely to MO, whereas peak LV basal rotational and strain rates were concomitant with transmitral peak-E (figure 4). Peak untwisting rate and peak LV diastolic apical rotational rate were correlated with IVRT (R=0.63, *P*<0.001 and R=0.48, *P*<0.001, respectively), while peak LV diastolic basal rotational rate and longitudinal and circumferential SR were related to peak-E (R=0.64, 0.79 and 0.81 respectively, *P*<0.001). The stepwise regression analysis shown that these mechanical events mainly explained the increase in peak-E with exercise intensity (table 4).

Mean UT_{IVRT} progressively increased from rest to W3 (table 5). %UT_{IVRT} decreased from rest to W1 (45.3 ± 22.5 *versus* 28.0 ± 15.4%, *P*=0.0003) then remained unchanged during exercise (from 28.0 ± 15.4 to 30.6 ± 16.6%, NS). Peak untwisting rate occurred during the IVR period at rest and was delayed after MO during exercise when the IVRT shortened (figure 4). UT_{IVRT} (deg) was stable from rest to W3 (between 3.5 ± 1.6 and 4.1 ± 2.1°, NS).

Twist-radial displacement loops (figure 5) indicated that exercise intensity did not affect the relationship between radial displacement and torsion during the cardiac cycle.
Systole was characterized by roughly linear relationship between torsion and radial displacement, and diastole by rapid untwisting before radial displacement.

**DISCUSSION**

This study based on STE reports comprehensive kinetics of LV systolic and diastolic strains and torsion and their relationship to diastolic filling at different submaximal exercise intensities in healthy sedentary subjects. The major findings of the study were (1) LV systolic twist increased progressively with exercise intensity, whereas systolic longitudinal strain remained unchanged after the first workload, underlining the key role of torsional “reserve” in systolic-diastolic-coupling during exercise (2) Increased diastolic untwist, paralleling enhanced systolic twist, was driven mainly by early apical rotation and determined early mitral valve opening, whereas basal rotation, longitudinal and circumferential diastolic strain rates were major determinants of increased early diastolic filling.

*The key role of LV torsional reserve in systolic-diastolic coupling during exercise*

Very few data are available regarding the kinetics of LV strains during an incremental exercise test. Using STE, we observed that whereas longitudinal strains remained unchanged after the first workload of 20% of maximal aerobic power (figure 1), LV circumferential strains, rotations and torsion increased regularly with exercise intensity. The underlying mechanisms responsible for this heterogeneous response of LV strains are not well understood. LV torsion result from a complex arrangement of myocardial fibers within the LV wall. Contraction of the opposite helically oriented fibers creates LV torsion which follows subepicardial layers because of their longer lever, and the progressive increase in
LV torsion during effort reflected a higher contribution of subepicardial versus subendocardial layers \(^{29}\). An explanation could be that subendocardial contractility could be blunted during effort due to its higher sensibility to local ischemia \(^{30}\). Another explanation could be based on the regular decrease in LV end-diastolic diameters observed with exercise intensity (figure 1). Indeed, a decrease in LV internal diameters improves the mechanical advantage of subepicardial layers \(^{29,31}\) that in turn could progressively enhance LV torsion during effort.

During the incremental exercise, the increase in LV untwisting rate was progressive and correlated to enhanced systolic torsion. The magnitude of increase was significantly higher for untwisting rate than for other mechanical components (table 3 and figure 3), confirming its key role when diastolic time shortens \(^{15-17}\). During diastole, whatever the exercise intensity, LV untwisting occurs earlier compared to LV normal strains, inducing an LV intraventricular pressure gradient that drives LV filling \(^{6}\). The extent of untwisting increase was highly significant even between W2 and W3, suggesting that there is still an «untwisting reserve» when exercise intensities are higher.

This important torsional reserve probably plays a key role in systolic-diastolic coupling during exercise: a decreased end-diastolic volume due to a shortened filling period could induce enhanced systolic LV twist, which in turn results in increased diastolic untwisting in order to enable rapid filling and thus support stroke volume. Previous study demonstrated the close functional relationship in normal patients \(^{6,17}\) between systolic twisting and early diastolic untwisting, generating ventricular recoil and negative intraventricular pressure gradient or suction. However, this is the first study reporting kinetics of torsional mechanics with increasing exercise intensities. Our results suggest that the contribution of LV torsional mechanics might become more important to LV filling as diastole shortens with increasing heart rates. Thus, the storage of energy during LV twist
which is released during early diastole seems to be a fundamental mechanism to support diastolic filling with increasing workloads.

*Unchanged timing of mechanical diastolic events*

The timing of diastolic mechanics are of major interest to better understand diastolic function, but studies in normal subjects according to exercise intensity are lacking 16, 17. Our results indicated that all time periods of the cardiac cycle were reduced proportionally with increasing heart rate (figure 4) and that the chronology of different diastolic mechanical events was respected when time was expressed in percentage of systolic duration. The time to peak untwisting rate during effort was not different from resting values and was not affected by exercise intensity (table 3 and figure 4). Diastolic untwisting always occurred close to MO, preceding peak diastolic longitudinal and circumferential SR which occurred close to transmitral peak-E (figure 4), as evidenced by the similar profile of the torsion-radial displacement loops during diastole at rest and during exercise (figure 5). The %UTIVRT decreased only from rest to W1, but was not further affected by exercise intensity. Very few studies reported %UTIVRT during effort. Notomi et al. 17 obtained similar results at a HR of 112 ± 10 bpm, whereas Esch et al. 16 did not found any difference between rest and effort in healthy young subjects. UTIVRT was approximately 4° at rest and whatever the exercise intensity (table 5), implying that a constant angle of untwist enabled a sufficient drop in LV pressure to MO. During effort, at end-systole, the atrio-ventricular pressure gradient is higher compared to resting values 32, suggest that, for a given elastic recoil (*i.e.* for a given untwisting angle), the drop in LV pressure is higher during effort.

*The specific roles of apical and basal rotations*
Previous studies documented that the LV apex rotates earlier than the LV base at rest \(^{16,17,33}\), but information on timing of LV rotational events during exercise is missing. Our results highlighted that this chronology was respected during effort (figure 4). Moreover, the difference between time to peak apical and basal rotation was majored when exercise intensity increased. Peak apical rotation occurred early in systole and time to peak shortened when exercise intensity increased (table 2), whereas peak basal rotation occurred after AC and time to peak remained constant during effort.

Consequently, during diastole, peak rotational rate occurred earlier at the apex, close to MO, whereas peak basal rotation occurred later, close to peak-\(E\). At rest and during incremental exercise, diastolic untwisting rate closely followed apical rotation and their peaks occurred closely to MO. Strong correlations were found between peak untwisting, diastolic apical rotational rate and IVRT, underlying their role for early MO when heart rate increases. Peak basal rotational rate appeared close to transmitral peak-E (table 3 and 5). Strong correlations were found between peak-E and peak basal rotational rate, and stepwise regression analysis (table 4) underlined that 57% of peak-E was determined by two main factors: peak basal rotational rate (which was the strongest predictor) and longitudinal SR.

Previous studies observed also an apex-to-base dispersion in regional timing of LV strain events \(^{34-36}\). The post systolic strains of basal regions, due in part to a higher electrical – mechanical delay \(^{37}\), has already been reported as an active mechanism enhancing the apex-to-base gradient of relaxation that facilitates rapid expansion of LV cavity near the apex, causing a rapid decrease of LV pressure during IVRT \(^{35}\). Our results demonstrated that this mechanism is also observed during effort.

**Clinical implications**
This is the first study reporting dynamics of LV torsion and strains during an incremental submaximal exercise test in healthy sedentary subjects. It gives new insights into physiologic adaptive mechanisms of myocardial mechanics to preserve stoke volume when diastolic time shortens during effort, underlining the key role of torsional “reserve” in systolic-diastolic coupling with increasing workloads.

This potential of STE to assess the kinetics of LV diastolic mechanics and their interaction with LV filling during an incremental exercise is of major interest to investigate LV diastolic dysfunction in various pathologic conditions. Previous studies documented altered torsional mechanics in aortic stenosis, hypertrophic cardiomyopathy and dilated cardiomyopathy, but subtle dysfunction might become more apparent with exercise. Few studies investigated LV torsion in patients at rest and at one single exercise load with a maximal heart rate ≤ 100 bpm. In heart failure patients with preserved ejection fraction LV twist failed to rise normally with exercise and diastolic untwisting rate was significantly lower compared to controls. In a study of 7 patients with hypertrophic cardiomyopathy, systolic torsion was higher in patients compared to controls at rest, but failed to increase normally with exercise, whereas untwisting was delayed and non-enhanced.

The possibility to follow dynamics of these variables at different submaximal exercise intensities in patients should allow better understanding of the underlying mechanisms of exercise intolerance. Besides altered relaxation and/or increased ventricular stiffness, altered untwisting should be considered as one possible mechanism contributing to exertional dyspnea.

Study limitations
The use of STE limits the frame rate so that strain mechanics can only be explored at submaximal exercise intensities. However STE, which has greater feasibility and reproducibility than tissue Doppler imaging, allowed timing of different mechanical events with sufficient accuracy for the explored exercise intensities and with a mean heart rates of 120 bpm at W3. Furthermore, stroke volume levelled off at W2 and remained unchanged between W2 and W3, so we can assume that major adaptive mechanisms during exercise took place during the 3 explored workloads. Previous studies indicated that exercise at 120-130 bpm was sufficient to detect diastolic dysfunction occurring during effort 12, 17.

The exact location of the basal and apical planes may be different from patient to patient. However, previous studies have validated the accuracy of STE versus tagged MRI 19 and care was taken to be at similar planes both at rest and during exercise.
ACKNOWLEDGMENTS

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DISCLOSURES

None.
REFERENCES


Table 1. Resting echocardiographic and blood pressure data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tr>
<td>Heart Rate, bpm</td>
<td>66 ± 9</td>
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<tr>
<td>Stroke volume, mL</td>
<td>99 ± 14</td>
</tr>
<tr>
<td>Cardiac output, L.min⁻¹</td>
<td>6.4 ± 1.4</td>
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<tr>
<td>Blood Pressure, mmHg</td>
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<tr>
<td>Systolic</td>
<td>127 ± 9</td>
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<tr>
<td>Diastolic</td>
<td>86 ± 7</td>
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<tr>
<td>LV-EDV, mL</td>
<td>132 ± 17</td>
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<tr>
<td>LV-ESV, mL</td>
<td>43 ± 8</td>
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<tr>
<td>IVST, cm</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>PWT, cm</td>
<td>0.9 ± 0.1</td>
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</table>

LV-EDV: Left ventricular end-diastolic volume; LV-ESV: Left ventricular end-systolic volume; IVST: Interventricular septum thickness; PWT: Posterior wall thickness.
Table 2. Time to peak of left ventricular strains, rotations and torsion

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Workload 1</th>
<th>Workload 2</th>
<th>Workload 3</th>
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<tbody>
<tr>
<td>Longitudinal strain, %</td>
<td>103 ± 8</td>
<td>103 ± 5</td>
<td>102 ± 6</td>
<td>100 ± 6</td>
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<tr>
<td>Circumferential strain, %</td>
<td>103 ± 8</td>
<td>104 ± 6</td>
<td>104 ± 6</td>
<td>104 ± 7</td>
</tr>
<tr>
<td>Basal rotation, %</td>
<td>108 ± 20</td>
<td>109 ± 13</td>
<td>109 ± 16</td>
<td>111 ± 17</td>
</tr>
<tr>
<td>Apical rotation, %</td>
<td>91 ± 7</td>
<td>89 ± 10</td>
<td>78 ± 18*</td>
<td>72 ± 18</td>
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<tr>
<td>Torsion, %</td>
<td>92 ± 4</td>
<td>93 ± 7</td>
<td>92 ± 5</td>
<td>92 ± 6</td>
</tr>
</tbody>
</table>

*: percentage of systolic duration
*: Significant difference from previous workload
Table 3. Peak and time to peak strain rates, rotational rates and untwisting rate during systole and diastole

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Workload 1</th>
<th>Workload 2</th>
<th>Workload 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systole</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Longitudinal strain rate, s(^{-1})</td>
<td><em>Peak</em> -0.96 ± 0.14 -1.36 ± 0.22* -1.51 ± 0.23* -1.75 ± 0.23*</td>
<td>-1.36 ± 0.22* -1.51 ± 0.23* -1.75 ± 0.23*</td>
<td>-1.49 ± 0.23* -1.86 ± 0.30* -1.98 ± 0.25*</td>
<td>-1.49 ± 0.23* -1.86 ± 0.30* -1.98 ± 0.25*</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 44 ± 11 43 ± 7 44 ± 7 39 ± 8</td>
<td>43 ± 7</td>
<td>44 ± 7</td>
<td>39 ± 8</td>
</tr>
<tr>
<td>Circumferential strain rate, s(^{-1})</td>
<td><em>Peak</em> -1.18 ± 0.15 -1.49 ± 0.23* -1.86 ± 0.30* -1.98 ± 0.25*</td>
<td>-1.49 ± 0.23* -1.86 ± 0.30* -1.98 ± 0.25*</td>
<td>-1.86 ± 0.30* -1.98 ± 0.25*</td>
<td>-1.98 ± 0.25*</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 46 ± 5 47 ± 7 46 ± 6 47 ± 9</td>
<td>47 ± 7</td>
<td>46 ± 6</td>
<td>47 ± 9</td>
</tr>
<tr>
<td>Basal rotational rate, deg.s(^{-1})</td>
<td><em>Peak</em> -72.0 ± 16.5 -92.2 ± 32.6* -107.5 ± 35.5* -117.7 ± 29.4</td>
<td>-92.2 ± 32.6* -107.5 ± 35.5* -117.7 ± 29.4</td>
<td>-107.5 ± 35.5* -117.7 ± 29.4</td>
<td>-117.7 ± 29.4</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 60 ± 9 65 ± 11* 66 ± 10 68 ± 11</td>
<td>65 ± 11*</td>
<td>66 ± 10</td>
<td>68 ± 11</td>
</tr>
<tr>
<td>Apical rotational rate, deg.s(^{-1})</td>
<td><em>Peak</em> 79.1 ± 16.8 105.8 ± 21.3* 117.5 ± 23.6 133.1 ± 23.7*</td>
<td>105.8 ± 21.3* 117.5 ± 23.6 133.1 ± 23.7*</td>
<td>117.5 ± 23.6 133.1 ± 23.7*</td>
<td>133.1 ± 23.7*</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 24 ± 4 23 ± 5 23 ± 5 23 ± 6</td>
<td>23 ± 5</td>
<td>23 ± 5</td>
<td>23 ± 6</td>
</tr>
<tr>
<td>Twisting rate, deg.s(^{-1})</td>
<td><em>Peak</em> 68.3 ± 15.6 97.1 ± 31.9* 114.9 ± 28.8* 124.1 ± 35.3</td>
<td>97.1 ± 31.9* 114.9 ± 28.8* 124.1 ± 35.3</td>
<td>114.9 ± 28.8* 124.1 ± 35.3</td>
<td>124.1 ± 35.3</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 56 ± 11 52 ± 18 55 ± 17 53 ± 18</td>
<td>52 ± 18</td>
<td>55 ± 17</td>
<td>53 ± 18</td>
</tr>
<tr>
<td><strong>Diastole</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Longitudinal strain rate, s(^{-1})</td>
<td><em>Peak</em> 1.24 ± 0.34 1.77 ± 0.36* 1.89 ± 0.36 1.95 ± 0.38</td>
<td>1.77 ± 0.36* 1.89 ± 0.36 1.95 ± 0.38</td>
<td>1.77 ± 0.36* 1.89 ± 0.36 1.95 ± 0.38</td>
<td>1.77 ± 0.36* 1.89 ± 0.36 1.95 ± 0.38</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 142 ± 6 143 ± 7 143 ± 8 143 ± 10</td>
<td>143 ± 7</td>
<td>143 ± 8</td>
<td>143 ± 10</td>
</tr>
<tr>
<td>Circumferential strain rate, s(^{-1})</td>
<td><em>Peak</em> 1.00 ± 0.14 1.42 ± 0.21* 1.79 ± 0.26* 1.87 ± 0.27</td>
<td>1.42 ± 0.21* 1.79 ± 0.26* 1.87 ± 0.27</td>
<td>1.42 ± 0.21* 1.79 ± 0.26* 1.87 ± 0.27</td>
<td>1.42 ± 0.21* 1.79 ± 0.26* 1.87 ± 0.27</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 145 ± 6 145 ± 8 146 ± 11</td>
<td>145 ± 8</td>
<td>146 ± 11</td>
<td>146 ± 12</td>
</tr>
<tr>
<td>Basal rotational rate, deg.s(^{-1})</td>
<td><em>Peak</em> 49.9 ± 18.3 79.1 ± 21.0* 90.8 ± 29.5* 109.2 ± 27.9*</td>
<td>79.1 ± 21.0* 90.8 ± 29.5* 109.2 ± 27.9*</td>
<td>79.1 ± 21.0* 90.8 ± 29.5* 109.2 ± 27.9*</td>
<td>79.1 ± 21.0* 90.8 ± 29.5* 109.2 ± 27.9*</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 135 ± 16 141 ± 18 144 ± 19 148 ± 21</td>
<td>141 ± 18</td>
<td>144 ± 19</td>
<td>148 ± 21</td>
</tr>
<tr>
<td>Apical rotational rate, deg.s(^{-1})</td>
<td><em>Peak</em> -78.5 ± 31.3 -115.1 ± 38.4* -139.5 ± 53.2* -167.3 ± 61.8*</td>
<td>-115.1 ± 38.4* -139.5 ± 53.2* -167.3 ± 61.8*</td>
<td>-115.1 ± 38.4* -139.5 ± 53.2* -167.3 ± 61.8*</td>
<td>-115.1 ± 38.4* -139.5 ± 53.2* -167.3 ± 61.8*</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 114 ± 10 119 ± 9 119 ± 6 114 ± 6</td>
<td>119 ± 9</td>
<td>119 ± 6</td>
<td>114 ± 6</td>
</tr>
<tr>
<td>Untwisting rate, deg.s(^{-1})</td>
<td><em>Peak</em> -88.7 ± 34.2 -119.3 ± 42.8* -157.1 ± 53.0* -182.9 ± 53.5*</td>
<td>-119.3 ± 42.8* -157.1 ± 53.0* -182.9 ± 53.5*</td>
<td>-119.3 ± 42.8* -157.1 ± 53.0* -182.9 ± 53.5*</td>
<td>-119.3 ± 42.8* -157.1 ± 53.0* -182.9 ± 53.5*</td>
</tr>
<tr>
<td></td>
<td><em>TTP</em> 119 ± 9 121 ± 7 122 ± 8 122 ± 7</td>
<td>121 ± 7</td>
<td>122 ± 8</td>
<td>122 ± 7</td>
</tr>
</tbody>
</table>

*: Significant difference from previous workload
Table 4. Stepwise multiple regression analysis

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Dependent variable</th>
<th>Peak-E</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R^2$</td>
<td>0.566</td>
<td></td>
</tr>
<tr>
<td>Coefficient</td>
<td>Standard Error</td>
<td>P value</td>
</tr>
<tr>
<td>LV peak diastolic basal rotational rate</td>
<td>0.003</td>
<td>0.001</td>
</tr>
<tr>
<td>LV peak diastolic longitudinal SR</td>
<td>0.231</td>
<td>0.055</td>
</tr>
</tbody>
</table>
Table 5. Left ventricular diastolic parameters

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Workload 1</th>
<th>Workload 2</th>
<th>Workload 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean UT&lt;sub&gt;IVRT&lt;/sub&gt;, deg.s&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>64.1 ± 28.8</td>
<td>76.9 ± 35.7</td>
<td>103.6 ± 47.7*</td>
<td>110.7 ± 47.6</td>
</tr>
<tr>
<td>UT&lt;sub&gt;IVRT&lt;/sub&gt;, deg</td>
<td>3.9 ± 1.5</td>
<td>3.5 ± 1.6</td>
<td>4.1 ± 2.1</td>
<td>3.8 ± 1.9</td>
</tr>
<tr>
<td>%UT&lt;sub&gt;IVRT&lt;/sub&gt;, %</td>
<td>45.3 ± 22.5</td>
<td>28.0 ± 15.4*</td>
<td>30.6 ± 16.6</td>
<td>29.8 ± 20.4</td>
</tr>
<tr>
<td>IVRT ms</td>
<td>66 ± 18</td>
<td>46 ± 13*</td>
<td>41 ± 12</td>
<td>35 ± 10</td>
</tr>
<tr>
<td>% systolic duration</td>
<td>20 ± 6</td>
<td>17 ± 5*</td>
<td>16 ± 5</td>
<td>15 ± 5</td>
</tr>
<tr>
<td>Time to transmitral peak-E ms</td>
<td>480 ± 33</td>
<td>394 ± 35*</td>
<td>364 ± 33*</td>
<td>342 ± 35*</td>
</tr>
<tr>
<td>% systolic duration</td>
<td>149 ± 9</td>
<td>149 ± 10</td>
<td>149 ± 10</td>
<td>151 ± 10</td>
</tr>
</tbody>
</table>

Mean UT<sub>IVRT</sub>: mean untwisting rate during IVRT, UT<sub>IVRT</sub>: untwisting angle during IVRT, %UT<sub>IVRT</sub>: percentage of untwisting during IVRT. IVRT: isovolumic relaxation time, ms: time in milliseconds, % systolic duration: time in percentage of systolic duration.

*: Significant difference from previous workload
FIGURE LEGENDS

Figure 1 – Kinetics of left ventricular end-diastolic (EDD), end-systolic diameters (ESD) and stroke volume. W1, workload 1; W2, workload 2; W3, workload 3. Significant difference: *.

Figure 2 – Kinetics of left ventricular systolic strains. W1, workload 1; W2, workload 2; W3, workload 3. Significant difference: *.

Figure 3 – Variation from resting condition to workload 1 ( ), workload 2 ( ) and workload 3 ( ) of myocardial SR and twist/untwist rate during systole and diastole. SRL, longitudinal strain rate; SRC, circumferential strain rate; TR/UTR, twist/untwist rate. Significant difference: *.

Figure 4 – Myocardial strain and twist/untwist rates averaged on 20 healthy subjects. Values are expressed in percentage of systolic and diastolic duration and scale to their respective duration. Black continuous line: twist/untwisting rate, dotted line: apical rotational rate, discontinuous dotted line: basal rotational rate, blue line: longitudinal SR, red line: circumferential SR. AO, aortic opening; Peak S, peak ejection velocity; AC, aortic valve closure; MO, mitral opening; Peak E, peak early filling velocity; End E, end of early filling.

Figure 5 – Twist-radial displacement loops. ED, end-diastole; ES, end-systole; □, aortic valve closure; ●, mitral opening; ■, peak untwisting rate. W1, workload 1; W2, workload 2; W3, workload 3.
Figure 1

Stroke volume (mL)

LV diameters (mm)

Rest W1 W2 W3 Rest W1 W2 W3

* * * *

EDD ESD

Figure 1
Figure 2

- **Longitudinal strain (%):**
  - Rest: -25
  - W1: -30
  - W2: -25
  - W3: -20

- **Circumferential strain (%):**
  - Rest: -15
  - W1: -20
  - W2: -25
  - W3: -30

- **Basal rotation (deg):**
  - Rest: 0
  - W1: -8
  - W2: -6
  - W3: -4

- **Apical rotation (deg):**
  - Rest: 10
  - W1: 6
  - W2: 8
  - W3: 12

*Significant difference compared to rest.*
Figure 3

Systole

Diastole

Difference from resting condition (%)
Kinetics of Left Ventricular Strains and Torsion During Incremental Exercise in Healthy Subjects: The Key Role of Torsional Mechanics for Systolic-Diastolic Coupling
Grégory Doucende, Iris Schuster, Thomas Rupp, Aliona Startun, Michel Dauzat, Philippe Obert and Stéphane Nottin

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