Left ventricular torsion and strain patterns in heart failure with normal ejection fraction are similar to age-related changes

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Aims We used speckle tracking echocardiography (STE) to make a comparison between the effects of ageing and of heart failure with normal ejection fraction (HfnEF) on left ventricular (LV) torsion and strain patterns.

Methods and results Forty patients with HfnEF, 27 young controls and 26 older controls, were prospectively recruited. All subjects underwent clinical examination, 12-lead electrocardiogram, pulmonary function test, echocardiogram, and metabolic exercise test. LV torsion increases with advancing age (older controls vs. young controls, 2.2\(\pm\)0.9 vs. 1.4\(\pm\)0.8\(^8\)/cm; \(P=0.03\)). Circumferential strain was enhanced in patients with HfnEF (24.7\(\pm\)4.7 vs. 20.0\(\pm\)4.9%; \(P=0.003\)). Rotational deformation delay (time difference between peak basal rotation and peak apical rotation), global circumferential strain, E-velocity deceleration time, and LV end-diastolic volume index were independent predictors of LV torsion. LV torsion and body mass index were independent predictors of LV untwist rate.

Conclusion Ageing is associated with increased LV torsion secondary to reduced rotational deformation delay and increased peak basal rotation. LV torsion and strain patterns in patients with HfnEF are similar to age-related changes apart from circumferential strain, which is enhanced in patients with HfnEF.

KEYWORDS
Torsion;
Untwisting;
Heart failure with normal ejection fraction;
Ageing;
Speckle tracking echocardiography

Introduction
Heart failure with normal ejection fraction (HfnEF) comprises approximately half of patients with clinical features of chronic heart failure,\(^1\) with hospital admission/re-admission rates and length of stay similar to that of patients with systolic heart failure.\(^2\) These patients are often overweight or obese elderly women who frequently have associated hypertension, diabetes, and/or coronary artery disease.\(^2\) The prevalence of HfnEF appears to be increasing, and mortality rate is only a little less than that of systolic heart failure.\(^1\) Many patients with HfnEF have diastolic dysfunction, a feature that is also commonly found in normal ageing.\(^3\) No study has attempted to directly compare the physiological changes in left ventricular (LV) torsion and untwist associated with ageing and those found in patients with HfnEF. This is important because of the potentially significant overlap in the two processes especially when it comes to diagnosis and understanding the pathophysiology of HfnEF. In this study, we aim to investigate what features of LV biomechanics, e.g. LV torsion and untwist as well as LV strains, are related to HfnEF and which are age-related changes. We used 2D ultrasound speckle tracking echocardiography (STE) to non-invasively evaluate LV torsion and untwist in young and older healthy volunteers as well as in patients with HfnEF. STE estimation of LV torsion has been shown to be concordant with those analysed by tagged magnetic resonance imaging (MRI).\(^4\) Metabolic exercise testing was used to objectively measure exercise capacity in patients with HfnEF and healthy controls.

Methods
Study participants
Patients with heart failure with normal ejection fraction
We studied 40 HfnEF patients prospectively and consecutively recruited from heart failure clinics. All study participants had clinical examination, 12-lead electrocardiogram, pulmonary function test, echocardiogram, and metabolic exercise test. All patients had signs and/or symptoms of heart failure with an LV ejection fraction >50% by transthoracic echocardiography and met the criteria...
of Yturralde and Gaasch for diastolic heart failure. Patients with severe pulmonary disease, significant valvular heart disease, atrial fibrillation, or evidence of hypertrophic cardiomyopathy were excluded similar to previous studies. Pulmonary function test was performed to identify patients with severe pulmonary disease. The investigations were performed at The University of Birmingham with the approval of the Research Ethics Committee. Informed consent was obtained from all subjects.

Healthy controls
We studied 53 healthy controls with no cardiac history, no hypertension or diabetes mellitus. Twenty-seven healthy controls were under the age of 50 years and they were classified as young controls; the remainder were classified as older controls (n = 26). All healthy controls had a normal clinical cardiovascular examination, 12-lead electrocardiogram, and metabolic exercise test. They were healthy volunteers from the community.

Metabolic exercise testing
The metabolic exercise testing was performed on a Schiller CS-200 Ergo-Spiro exercise machine which was calibrated before every study. Subjects underwent spirometry and this was followed by symptom-limited erect treadmill exercise testing using incremental ramp protocol (speed and inclination were increased every minute) with simultaneous respiratory gas analysis. Samplings of expired gases were performed continuously, and data were expressed as 30 s means. Minute ventilation (VE/VCO2 slope), oxygen consumption, carbon dioxide production, and respiratory exchange ratio (RER) were obtained. Peak oxygen consumption (VO2max) was defined as the highest value of oxygen consumption measured during the exercise period. Blood pressure and ECG were monitored throughout. Subjects were encouraged to exercise to exhaustion with a minimal requirement of RER > 1.

Resting echocardiography
Echocardiography was performed with participants in the left lateral decubitus position with a Vivid 7 echocardiographic machine and a 2.5 MHz transducer. Resting scans were acquired in standard apical four-chamber and apical two-chamber views. All echocardiographic measurements were averaged from three heart beats. LV ejection fraction was calculated from LV volumes [LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV)] by the modified biplane Simpson rule in accordance with the guidelines. LVEDV and LVESV were indexed to body surface area (BSA). From the LV-inflow pattern (measured at the tips of the mitral valve), peak early (E) and late (A) filling velocities, E/A ratio, and E-velocity deceleration time (DCt) were measured. The isovolumic relaxation time (IVRT) was determined using pulsed-wave Doppler velocity data of the LV inflow. Tissue Doppler was applied end-expiratory in the pulsed-wave Doppler mode at the level of the lateral mitral annulus from an apical four-chamber view. The velocities of early diastolic wave (E’) was noted. Lateral mitral annulus velocities were recorded to derive E/E’. Parasternal circular short-axis images were taken at three distinct levels: LV basal level with the cross-section as circular as possible (identified by the mitral valve), papillary and apical (no papillary muscles present) similar to previous studies. Area-length method was used to determine LV mass indexed to BSA. LV hypertrophy was defined as an LV mass indexed to BSA that exceeded 88 g/m2 for women and 102 g/m2 for men.

Speckle tracking echocardiography
STE was measured using a commercially available speckle tracking system in an ECHOPAC (ver. 4.2.0, GE, USA) workstation. Myocardial deformation measurements were performed using tissue speckle tracking. In this system, the displacement of speckles of myocardium in each spot was analysed and tracked from frame to frame. We selected the best quality digital 2D image cardiac cycle, and the left ventricle endocardium was traced at end-systole. The width of the region of interest was adjusted as required to fit the wall thickness. The software package then automatically tracked the motion through the rest of the cardiac cycle. The onset of QRS complex was taken as the beginning of systole. To adjust for intra- and inter-subject differences in heart rate, all time intervals were normalized to R-R interval by expressing the time interval as a percentage of the R-R interval (\%R). Adequate tracking was verified in real time. Regarding adequate tracking quality, the system (ECHOPAC, ver. 4.2.0, GE, USA) automatically generates an acceptable or unacceptable tracking quality. We systematically accepted only segments that received an acceptable tracking quality for analysis with visual control of tracking quality to ensure adequate automatic tracking. This was done by verifying adequate tracking quality of endocardial and epicardial borders by the system. To optimize speckle tracking, 2D grey-scale harmonic images were obtained at a frame rate of 70-100 frames/s. For each subject, longitudinal strain values for all LV myocardial segments in each of the apical four- and two-chamber views were measured and averaged to derive the global LV longitudinal strain, strain rates, and velocity. Circumferential strain values were obtained in all 18 segments of the three short-axis views. The average of peak systolic circumferential strain values from the three short-axis views was calculated to derive the global LV circumferential strain and strain rates. Similarly, peak radial strain values were measured in all 18 segments at the three short-axis views and averaged to derive the global radial strain and strain rates.

In addition, cardiac rotation was computed using speckle tracking. Counter-clockwise rotation was marked as a positive value and clockwise rotation as a negative value when viewed from the apex. In order to calculate LV torsion and LV untwist and untwist rates, the rotation traces of the basal and apical LV cross-sections were exported into DPlot graph software (Version 2.2.1.4, HydeSoft Computing, LLC, Vicksburg, MS, USA). The LV twist curve was generated by calculating the difference between apical and basal rotations at each corresponding time point. LV twist rates were derived from the first derivative of the LV twist curve. Peak LV torsion was derived from LV twist divided by LV diastolic longitudinal length as described previously. Rotational deformation delay was also determined and defined as the magnitude of the time difference between time-to-peak basal rotation and time-to-peak apical rotation. Peak untwist rate at the E-wave was used to determine peak untwist rate as described in previous studies. Of the 93 subjects in the study, 63 (68%) subjects had both adequate LV basal and apical images for speckle tracking to complete analysis of all LV rotational parameters, which is comparable to previous studies.

Reproducibility of speckle tracking echocardiography
Inter-observer measurement variability was determined by two independent observers who measured LV torsion in 10 randomly selected controls. To obtain the intra-observer variability, the first observer performed the analysis at two separate occasions at 1 month apart. We performed Bland–Altman plots to assess reproducibility of measurement. Our results showed that for LV torsion, intra-observer reproducibility was \(0.24 \pm 0.58\) [bias \(0.19\) standard deviation of the difference (STD)] with a mean of 3.06 and 2.82 / cm. Inter-observer reproducibility was \(0.15 \pm 0.69\) (bias \(0.19\)  STD) with a mean of 2.82 and 2.67 / cm.

Statistics
Continuous variables are expressed as means ± SD. Comparisons were performed with one-way ANOVA if the data were normally distributed. Categorical variables were compared with Pearson’s \(\chi^2\) test. A P-value of < 0.05 was considered to indicate statistical
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Table 1  Baseline clinical characteristics and metabolic exercise parameters of the study population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Young (n = 27)</th>
<th>Older (n = 26)</th>
<th>HfEF (n = 40)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>30 ± 8</td>
<td>64 ± 7*</td>
<td>67 ± 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender, %</td>
<td>7 (26)</td>
<td>14 (54)*</td>
<td>29 (73)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25 ± 3</td>
<td>26 ± 5</td>
<td>30 ± 4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVH, n (%)</td>
<td>0</td>
<td>5 (19)</td>
<td>15 (38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAD, n (%)</td>
<td>0</td>
<td>4 (10)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>0</td>
<td>0</td>
<td>2 (5)</td>
<td>NA</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>0</td>
<td>0</td>
<td>29 (73)</td>
<td>NA</td>
</tr>
<tr>
<td>Medication, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>0</td>
<td>0</td>
<td>13 (33)</td>
<td>NA</td>
</tr>
<tr>
<td>ACE-I or ARB</td>
<td>0</td>
<td>0</td>
<td>26 (65)</td>
<td>NA</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>0</td>
<td>0</td>
<td>7 (18)</td>
<td>NA</td>
</tr>
<tr>
<td>Nitrites</td>
<td>0</td>
<td>0</td>
<td>3 (8)</td>
<td>NA</td>
</tr>
<tr>
<td>Calcium antagonist</td>
<td>0</td>
<td>0</td>
<td>12 (30)</td>
<td>NA</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>0</td>
<td>0</td>
<td>14 (35)</td>
<td>NA</td>
</tr>
<tr>
<td>Statins</td>
<td>0</td>
<td>0</td>
<td>21 (53)</td>
<td>NA</td>
</tr>
<tr>
<td>Resting heart rate, bpm</td>
<td>78 ± 10</td>
<td>82 ± 16</td>
<td>79 ± 15</td>
<td>0.498</td>
</tr>
<tr>
<td>Resting SBP, mmHg</td>
<td>114 ± 10</td>
<td>132 ± 22*</td>
<td>137 ± 21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resting DBP, mmHg</td>
<td>72 ± 6</td>
<td>82 ± 11*</td>
<td>82 ± 11</td>
<td>0.002</td>
</tr>
<tr>
<td>VO₂max, mL/kg/min</td>
<td>44 ± 7</td>
<td>35 ± 8*</td>
<td>21 ± 5*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RER</td>
<td>1.28 ± 0.11</td>
<td>1.12 ± 0.10*</td>
<td>1.07 ± 0.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VE/VO₂</td>
<td>28 ± 4</td>
<td>28 ± 7</td>
<td>33 ± 6*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Breathing reserve, L/min</td>
<td>52 ± 6</td>
<td>44 ± 3</td>
<td>36 ± 15</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak SBP, mmHg</td>
<td>169 ± 19</td>
<td>191 ± 27*</td>
<td>183 ± 26</td>
<td>0.012</td>
</tr>
<tr>
<td>Peak DBP, mmHg</td>
<td>74 ± 10</td>
<td>84 ± 10*</td>
<td>83 ± 13</td>
<td>0.004</td>
</tr>
<tr>
<td>Peak heart rate, bpm</td>
<td>178 ± 11</td>
<td>164 ± 11*</td>
<td>136 ± 19**</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data expressed as mean ± SD.

BMI, body mass index; CAD, coronary artery disease; DBP, diastolic blood pressure; LVH, left ventricular hypertrophy; RER, respiratory exchange ratio; SBP, systolic blood pressure.

*P < 0.05 vs. young group.

**P < 0.05 vs. older group.

Results

Patient characteristics

Patients with HfEF were generally females, overweight, mean age of 67 ± 10 with a high prevalence of hypertension, which has been similarly described in previous large epidemiological studies.2 HfEF patients also had significantly reduced VO₂max and reduced peak HR on metabolic exercise testing compared with older controls (Table 1). The E/E’ at the lateral mitral annulus was significantly higher in patients than in older controls (Table 2).

Longitudinal, radial, and circumferential strains

Ageing

Global longitudinal, radial, and circumferential strains were preserved with advancing age. However, longitudinal strain rate $E$ was lower and longitudinal strain rate $A$ was higher with ageing. Longitudinal velocity (peak 5 and $E$) was also significantly reduced with ageing (Table 3).

Heart failure with normal ejection fraction

Compared with older controls, global longitudinal and radial strains were preserved in patients with HfEF. Longitudinal strain rates and velocity were also comparable to older controls. However, global circumferential strain was significantly increased in patients with HfEF compared with older controls ($-24.7 ± 4.7$ and $-20.0 ± 4.9$, respectively, $P = 0.003$). Global circumferential strain rate peak $S$ and $E$ were significantly higher in HfEF patients compared with older controls.

Left ventricular torsion and untwist rate

Aging

LV torsion is significantly increased with ageing (Table 4). This is in part due to the time-to-peak apical rotation occurring later during systole with ageing, with the resulting trend of peak rotational deformation delay decreasing with advancing age ($P = 0.07$), as well as a trend for increased LV basal rotation with ageing ($P = 0.07$). Peak LV untwist rate was preserved with ageing and thus the times to 15, 25, 50, and 75% untwist were not significantly delayed with ageing.

Heart failure with normal ejection fraction

Compared with older controls, LV torsion and peak untwist rate were preserved in patients with HfEF. Peak rotational deformation delay was similar in HfEF and older controls. Furthermore, the times to 15, 25, 50, and 75% untwist...
were not delayed in HfNEF patients when compared with older controls. (Figure 1).

**Associations with left ventricular torsion**

On univariate analysis, LV torsion was significantly correlated with age, BMI, DcT, E/A ratio, E/E′, LVEDV index, LVESV index, LV mass index, VO\textsubscript{2}\textsuperscript{max}, global radial strain, global circumferential strain, rotational deformation delay, and peak LV torsion. In the multivariate analysis, a linear regression model was used to examine LV untwist as the dependent variable and found that LV torsion and BMI were independent predictors of LV untwist rate ($r^2 = 0.65$, $P < 0.001$ and $P = 0.013$, respectively).

**Discussion**

The principal findings of the present study are: (i) LV torsion increases with advancing age due in part to reduced rotational deformation delay and increased LV basal rotation; however, LV torsion is unchanged in HfNEF compared with older controls; (ii) LV untwist and peak untwist rates and LV longitudinal and radial strains are preserved with ageing and in patients with HfNEF; (iii) circumferential strain and strain rate are enhanced in patients with HfNEF; (iv) LV torsion is independently predicted by rotational...
Left ventricular torsion and strain patterns in heart failure

Table 4  Left ventricular torsion and untwist

<table>
<thead>
<tr>
<th>Variables</th>
<th>Young</th>
<th>Older</th>
<th>HfnEF</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak apical rotation, °</td>
<td>8.5 ± 4.6</td>
<td>8.8 ± 5.1</td>
<td>10.4 ± 5.4</td>
<td>0.380</td>
</tr>
<tr>
<td>Time to peak apical rotation, %RR</td>
<td>33 ± 12</td>
<td>42 ± 6</td>
<td>41 ± 8</td>
<td>0.002</td>
</tr>
<tr>
<td>Peak basal rotation, °</td>
<td>-4.7 ± 2.6</td>
<td>-7.5 ± 2.7</td>
<td>-7.4 ± 5.0</td>
<td>0.025</td>
</tr>
<tr>
<td>Time to peak basal rotation, %RR</td>
<td>43 ± 14</td>
<td>43 ± 11</td>
<td>34 ± 10</td>
<td>0.034</td>
</tr>
<tr>
<td>Peak rotational deformation delay, %RR</td>
<td>19 ± 14</td>
<td>11 ± 9</td>
<td>10 ± 8</td>
<td>0.010</td>
</tr>
<tr>
<td>Peak torsion, °/cm</td>
<td>1.4 ± 0.8</td>
<td>2.2 ± 0.9*</td>
<td>2.5 ± 1.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Time to peak torsion, %RR</td>
<td>38 ± 8</td>
<td>39 ± 4</td>
<td>40 ± 7</td>
<td>0.870</td>
</tr>
<tr>
<td>Peak twist rate S, °/s</td>
<td>83 ± 41</td>
<td>111 ± 51</td>
<td>111 ± 46</td>
<td>0.066</td>
</tr>
<tr>
<td>Time to peak twist rate S, %RR</td>
<td>19 ± 12</td>
<td>17 ± 7</td>
<td>22 ± 9</td>
<td>0.222</td>
</tr>
<tr>
<td>Peak untwist rate E, °/s</td>
<td>-79.5 ± 40</td>
<td>-110 ± 35</td>
<td>-129 ± 55</td>
<td>0.002</td>
</tr>
<tr>
<td>Time to peak untwist rate E, %RR</td>
<td>49 ± 7</td>
<td>54 ± 8</td>
<td>53 ± 9</td>
<td>0.154</td>
</tr>
<tr>
<td>Time to 15% untwist, %RR</td>
<td>45 ± 7</td>
<td>48 ± 7</td>
<td>45 ± 6</td>
<td>0.361</td>
</tr>
<tr>
<td>Time to 25% untwist, %RR</td>
<td>47 ± 7</td>
<td>51 ± 7</td>
<td>48 ± 7</td>
<td>0.184</td>
</tr>
<tr>
<td>Time to 50% untwist, %RR</td>
<td>53 ± 11</td>
<td>61 ± 14</td>
<td>56 ± 10</td>
<td>0.148</td>
</tr>
<tr>
<td>Time to 75% untwist, %RR</td>
<td>62 ± 16</td>
<td>75 ± 18</td>
<td>73 ± 18</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Data expressed as mean ± SD.
%RR, % of R-R interval.
*P < 0.05 vs. young group.
**P < 0.05 vs. older group.

deforation delay, circumferential strain, and MV deceleration time; (v) LV untwisting rate is independently determined by peak LV torsion and by BMI.

LV torsion is the net result of counter-clockwise rotation of the base with respect to clockwise rotation of the apex along the LV long axis. Normal LV torsion is a component of systolic function and contributes to an energy-efficient ejection. The subsequent LV untwisting is a key determinant of diastolic function because it helps to generate the intra-ventricular pressure gradient (IVPG) during isovolumic relaxation, thus creating a suction effect to allow early diastolic filling to occur once the mitral valve opens. In this study, we found LV torsion increased with ageing consistent with previous STE studies and tagged MRI studies. The reason for this increased LV torsion is unclear but in patients with aortic stenosis and hypertrophic cardiomyopathy, where LV torsion is also enhanced, the explanation appears to be related to under-perfusion of the sub-endocardium, leading to reduced sub-endocardial myofibre functions, which normally counteracts the LV twisting generated by the sub-epicardial myofibres. In a tagged MRI study, ageing was associated with a decrease of contractile function in the sub-endocardium relative to that in the sub-epicardium without changes in ejection fraction. This impairment of sub-endocardial contractile function may be secondary to sub-endocardial fibrosis, asymptomatic sub-endocardial infarction, or reduced sub-endocardial perfusion. The net effect is increased LV torsion and the preservation of EF in the elderly and to reduce myocardial oxygen demand.

In addition, since LV torsion is determined by instantaneous basal and apical rotation, any changes in the magnitude of rotational deformation delay between apex and the base of the LV will affect LV torsion. Indeed, we found that LV torsion is independently predicted by rotational deformation delay as well as circumferential strain. We found in young controls that the peak apical rotation occurs earlier than peak basal apical rotation, which may be explained by the start of electrical activation sub-endocardially in the right-handed helix near the apical septum with subsequent spread of the electrical activity towards the base. The reduction of rotational deformation delay with ageing resulted in greater LV torsion. This appears to be primarily because time-to-peak apical rotation occurs later in systole and closer to the timing of peak basal rotation with advancing age. The reason why peak apical rotation occurs later in systole and close to the timing of peak basal rotation still remains to be investigated but some have postulated that it may be due to an increase in elastic and collagenous tissue in the conduction system with ageing and also due to prolonged contraction duration (prolonged active state). Other studies have indicated that the increase in LV torsion with ageing is related to significantly increased peak apical rotation.

In this study, we found that patients with HfnEF had preserved LV torsion and untwisting rate compared with older controls, at least at rest, which is consistent with previous studies. In a study involving a heterogeneous group of patients with diastolic dysfunction (e.g. hypertrophic cardiomyopathy, hypertension, and amyloidosis), LV twist and untwist rates were found to be significantly increased in patients with mild diastolic dysfunction. However, in patients with advanced diastolic dysfunction with increased filling pressure, LV torsion was normalized or reduced. In addition, we found LV torsion to be an independent predictor of LV untwisting rate. This is perhaps not surprising considering ventricular torsion during systole provides the potential energy for the later subsequent rapid untwisting recoil, and therefore the greater the LV torsion the more potential energy is stored for subsequent higher LV untwisting rate. Interestingly, peak LV untwisting rate has been found to be an independent predictor of the time constant of isovolumic relaxation (τ) and IVPG. It is possible therefore for the observed increased LV torsion (therefore increased potential energy for subsequent LV untwisting recoil) to be a compensatory mechanism for reduced ventricular relaxation associated with ageing. In patients with HfnEF, ventricular relaxation is also impaired compared...
with matched controls. In this study, we find untwisting rate to be preserved with HfnEF compared with older controls, which would suggest that LV untwisting becomes dissociated from LV relaxation rate in this population. Indeed, in patients with HfnEF, ‹ does not correlate with untwisting rate. Furthermore, we found that untwisting is not delayed with ageing or in patients with HfnEF (compared with older controls), which is reflected by the lack of significant differences in LV untwisting rate. We also found LV longitudinal and radial strains to be preserved with ageing and in patients with HfnEF (compared with older controls).

In this study, we found that patients with HfnEF have reduced VO2max and higher VE/VCO2 slope compared with older controls, which is supported by previous reports. Indeed, VE/VCO2 slope has been shown to have prognostic value in patients with diastolic heart failure with respect to mortality and hospitalization. Furthermore, we demonstrated that patients with HfnEF had increased circumferential strain and strain rate compared with older controls and that this was an independent predictor of LV torsion. It may be that circumferential strain is a marker of compensation to sustain LV torsion in order to preserve ejection fraction in these patients with HfnEF.

What we learn from this study is that many of the changes in LV biomechanics (e.g. LV torsion and untwist) in HfnEF are also present in older controls at rest. The parameters that do separate the two groups (i.e. patients and older controls) are the enhanced circumferential strain and strain rate as well as marker of increased LV end-diastolic pressure such as E/E'. During exercise, patients with HfnEF and similar age controls can be clearly differentiated by VO2max and VE/VCO2 slopes. It is possible that the pathophysiology of HfnEF is a dynamic process with marked changes occurring on exercise and that studying these patients at rest might not be informative. Thus, to fully appreciate the role of LV torsion and untwist in the pathophysiology of HfnEF, we...
believe that patients with HfNEF need to be investigated under exercise conditions.

Study limitations

Our study is limited by the relatively small sample size. There were a slightly greater proportion of females in the HfNEF group vs. the older control group, but the differences were relatively small and would not be expected to influence the results significantly. Statistically, there were no differences in age between the HfNEF group and the older control group. A small proportion of patients had coronary artery disease, which may have affected LV mechanics; however, coronary artery disease is common in HfNEF and thus is part of the syndrome. A proportion of patients with HfNEF were on medications which may affect LV function; however, they would be expected to affect all strain parameters, not selective ones.

Conclusions

Ageing is associated with increased LV torsion secondary to reduced rotational deformation delay and increased peak basal rotation. LV untwist rate and longitudinal and radial strains are preserved with ageing. LV torsion and strain patterns in patients with HfNEF are similar to age-related changes apart from circumferential strain, which is enhanced in patients with HfNEF. Independent determinant of LV torsion are rotational deformation delay, circumferential strain, LVEDV index, and MV deceleration time, and LV untwist rate is independently predicted by peak LV torsion and BMI.

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