Age, Sex, and Hypertension-Related Remodeling Influences Left Ventricular Torsion Assessed by Tagged Cardiac Magnetic Resonance in Asymptomatic Individuals

The Multi-Ethnic Study of Atherosclerosis

Kihei Yoneyama, MD, PhD; Ola Gjesdal, MD, PhD; Eui-Young Choi, MD, PhD; Colin O. Wu, PhD; W. Gregory Hundley, MD; Antoinette S. Gomes, MD; Chia-Ying Liu, PhD; Robyn L. McClelland, PhD; David A. Bluemke, MD, PhD; Joao A.C. Lima, MD

Background—The aim of the present study was to evaluate how torsion is influenced by left ventricular (LV) remodeling associated with age, sex, and hypertension in a large community-based population.

Methods and Results—Myocardial shortening and torsion were assessed by tagged cardiac magnetic resonance in 1478 participants without clinically apparent cardiovascular disease in the Multi-Ethnic Study of Atherosclerosis (MESA). Torsion was defined as the difference between apical and basal rotation divided by slice distance. In multivariable linear regression models, older age was associated with lower stroke volume (−3.6 mL per decade; P<0.001) and higher LV mass-to-volume ratio (0.03 g/mL per decade; P<0.001), along with lower circumferential shortening (−0.17% per decade; P<0.05). Torsion, however, was greater at older ages (0.14° per decade; P<0.001) and in women (0.37°/cm versus men; P<0.001). Hypertensive participants had higher LV mass and LV mass-to-volume ratio (15.5 g and 0.07 g/mL, respectively; P<0.001 for both). Circumferential shortening was lower in hypertensive (−0.42%; P<0.01), whereas torsion was higher after adjustment for age and sex (0.17°/cm; P<0.05).

Conclusions—Older age is associated with lower LV volumes and greater relative wall thickness and is accompanied by lower circumferential myocardial shortening, whereas torsion is greater with older age. Hypertensive individuals have greater LV volumes and relative wall thickness and lower circumferential shortening. Torsion, however, is greater in hypertension independently of age and sex. Torsion may therefore represent a compensatory mechanism to maintain an adequate stroke volume and cardiac output in the face of the progressively reduced LV volumes and myocardial shortening associated with hypertension and aging. (Circulation. 2012;126:2481-2490.)

Key Words: aging ▪ blood pressure ▪ cardiac function ▪ cardiac output ▪ hypertrophy ▪ magnetic resonance imaging ▪ ventricular remodeling

Epidemiological studies report that 40% to 50% of patients with heart failure have preserved ejection fraction,1,2 and the prevalence of heart failure with preserved ejection fraction increases with age, especially in women.2 Hypertension increases with age and represents one of the most important risk factors for heart failure; it increases wall thickness in response to elevated blood pressure (BP) as a compensatory mechanism to minimize wall stress.3 However, alterations of left ventricular (LV) structure and function associated with hypertension, independently of age and sex, are not entirely understood. These observations suggest that LV function changes with age and sex and that hypertension may predispose to heart failure.

Clinical Perspective on p 2490

LV systolic deformation is a complex 3-dimensional phenomenon characterized by circumferential shortening (CS), longitudinal shortening, radial thickening, and ventricular torque for the purpose of ejecting blood from the LV into the aorta under pressure. Critical to enabling LV systolic deformation, the orientation of myofibers changes smoothly across the LV wall from a left-handed helix in the subepicardium to

Received January 1, 2012; accepted September 17, 2012.

From the Department of Cardiology, Johns Hopkins University, Baltimore, MD (K.Y., O.G., E.-Y.C., C.-Y.L., J.A.C.L.); Offices of Biostatistics Research, National Heart, Lung and Blood Institute, Bethesda, MD (C.O.W.); Department of Internal Medicine/Cardiology, Wake Forest University Health Sciences, Winston-Salem, NC (W.G.H.); Department of Radiology, UCLA School of Medicine, Los Angeles, CA (A.S.G.); Department of Biostatistics, University of Washington, Seattle (R.L.M.); and National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health Clinical Center, Bethesda, MD (D.A.B.).

Correspondence to Joao A.C. Lima, MD, FACC, Johns Hopkins University, Blalock 524D1, Johns Hopkins Hospital, 600 N Wolfe St, Baltimore, MD 21287. E-mail jlima@jhmi.edu

© 2012 American Heart Association, Inc.

Circulation is available at http://circ.ahajournals.org DOI: 10.1161/CIRCULATIONAHA.112.093146

2481
a circumferential orientation in the mid wall to a right-handed helix in the subendocardium.4–6 During ejection, the subendocardial and subepicardial layers shorten simultaneously, resulting in rotation of the apex and base in the counterclockwise and clockwise directions, respectively, when viewed from the apex.7 LV systolic torsion limits myocardial energy consumption and minimizes transmural fiber stress gradients and oxygen demand, resulting in a more efficient LV contraction.4,8–10 During isovolumic relaxation, torsional unfolding occurs and contributes to diastolic suction and a reduction in LV pressure.5,7 Thus, torsion and unfolding are considered to be important indicators of cardiac performance, and LV hypertrophy and fibrosis associated with hypertension could result in significant alterations of LV torque. It has previously been suggested that higher LV systolic wringing motion is found in the elderly11–14; however, study sample sizes were small. Therefore, torsion has not been previously evaluated in a large cohort study. In addition, the assessment of torsional deformation by echocardiography is methodologically challenging because the distance between the basal and the apical short-axis slices is difficult to assess accurately by echocardiography.

Tagged cardiac magnetic resonance (CMR) provides accurate information on the slice distance and is commonly used as the gold standard method for cardiac deformation assessment.15–17 Because the rotation gradient has been reported to be nearly linear from the LV base to apex,15,18 torsion can be accurately expressed as twist normalized by slice distance. The aim of the present study was to evaluate how torsion is influenced by LV remodeling associated with age, sex, and hypertension in a large community-based multiethnic population.

Methods

Participants

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective study designed to evaluate mechanisms that underlie the development and progression of subclinical cardiovascular diseases among asymptomatic individuals in the general population. Details of the MESA study design have been given previously.19 In brief, between July 2000 and August 2002, 6814 men and women who identified themselves as white, black, Hispanic, or Chinese and were 45 to 84 years of age and free of clinically apparent cardiovascular disease were recruited. CMR was performed in 5004 participants as part of the baseline examination. In this ancillary study, 1773 consecutive participants underwent tagged CMR studies at enrollment in 6 centers (Wake Forest University, Columbia University, Johns Hopkins University, University of Minnesota, Northwestern University, and University of California). The participants in the tagged CMR study were randomly selected. Results of 295 participants (16.6%) were excluded because of technical issues or poor-quality or missing slice acquisition at either the basal or apical level. Thus, a total of 1478 participants were enrolled in the study. All participants gave informed consent for the study protocol, which was approved by the institutional review boards of all MESA field centers and the CMR reading center.

MRI Protocol

Baseline CMR images were acquired with 1.5-T MR scanners (Signa LX or CVi, GE Medical Systems, Waukesha, WI; Symphony or Sonata, Siemens Medical Systems, Erlangen, Germany). After acquisition of standard scout images, 2- and 4-chamber cine MR images were acquired with the use of steady-state free-precession imaging sequences. Short-axis cine images were then obtained with retrospective gating with a temporal resolution of ≤50 milliseconds from above the mitral valve plane to the LV apex. Three tagged short-axis slices (base to apex) were obtained with an image plane distance of 5 to 8 mm. Parallel striped tags were prescribed in 2 orthogonal orientations (0° and 90°) with ECG-triggered fast gradient echo sequence with spatial modulation of magnetization. Parameters for tagged images were as follows: field of view, 40 cm; slice thickness, 8 to 10 mm; repetition time, 6 milliseconds; echo time, 3.0 milliseconds; flip angle, 10° to 12°; matrix, 205×128 with Siemens scanner and 128×64 with GE scanners; temporal resolution, 20 to 41 milliseconds; and tag spacing, 7 mm. The detailed protocol for the tagged CMR studies has previously been described.6

MRI Data Analysis

LV end-systolic volume, LV end-diastolic volume (LVEDV), stroke volume (SV), LV mass, and LV ejection fraction were measured with commercially available software (MASS 4.2; MEDIS, Leiden, the Netherlands), as previously described.20,21 In short, the endocardial and epicardial myocardial borders were contoured by use of a semiautomated method. The difference between the epicardial and endocardial areas for all slices was multiplied by slice thickness and section area to then be normalized by the specific myocardial density (1.04 g/mL) to determine the LV mass. LV mass index was defined as LV mass divided by height to the power of 1.7.22 The mass-to-volume (M/V) ratio was calculated as LV mass divided by LVEDV. LV length at end diastole was calculated as the average distance from the epicardial apex to the mitral valve insertion measured from the 2- and 4-chamber views. LV sphericity index at end diastole was calculated as the percentage of the LVEDV relative to the volume of a calculated sphere with the LV length.23 A higher index represents a more spherical shape of the ventricle.

Rotation and Myocardial Strain Analyses

Rotation and CS were assessed in short-axis tagged slices with HARP software (Harmonic Phase; Diagnosoft, Palo Alto, CA). Endocardial and epicardial contours were traced manually on the image corresponding to the remaining cardiac phases automatically. Tagged images and rotation, twist, and torsion curves were assessed as illustrated in Figure 1A. Rotation (in degrees) was defined for each short-axis slice as average angular displacement in the LV midwall layer. During normal systole, the basal rotates in a clockwise direction and the apex in a counterclockwise direction when viewed from the LV apex. Normal apical rotation is by definition positive; twist (in degrees) was calculated as the net difference between apical and basal rotation angles for each frame during the cardiac cycle with MATLAB (MathWorks, Natick, MA). To normalize twist for slice distance, torsion (in degrees per 1 cm) was calculated by dividing peak systolic twist by the interslice distance (h; in centimeters).24 The distance h was calculated as the sum of 1 image plane thickness and the gap between planes. CS was represented by the absolute peak strain value and determined and averaged from 4 LV segments (anterior, lateral, inferior, and septal) from the LV midwall layer on the midventricular slice. Positive numbers represent more shortening. The ratio between torsion and SV (T/TSV) was calculated to estimate the effect of torsion compensation with LV volume change, as shown by the slope during systole in torsion-volume loop, as described by Notomi et al.25 A higher ratio represents a higher torsion or compensation for lower SV. The torsion-to-CS (T/CS) ratio was calculated to estimate the slope of the relation between torsion and circumferential strain during the ejection period, as described by Lumens et al.26 This ratio describes subendocardial function, and dysfunction causes the ratio to increase.27

Risk Factor Measures

Standardized questionnaires were used to obtain information about smoking history and medication use and for history of high BP, high cholesterol, and diabetes mellitus. Smoking was defined as current, former, or never. Participant’s height and weight were measured, and resting BP was measured 3 times with participants in the seated position with a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon; GE Healthcare, Waukesha, WI). The
average of the last 2 measurements was used. Pulse pressure was calculated as systolic BP minus diastolic BP. Total cholesterol and glucose levels were measured from blood samples obtained after a 12-hour fast. Diabetes mellitus was defined as fasting glucose \( \geq 126 \text{ mg/dL} \) or the use of hypoglycemic medication or insulin. Hypertension was classified according to the seventh report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension was classified according to the seventh report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure. Glomerular filtration rate was estimated as previously described.

**Statistical Analysis**

Summary statistics were presented using mean±SD for continuous variables and percents for categorical variables. Nonparametric Wilcoxon-type trend tests for ordered groups were used to test the trends of continuously measured clinical characteristics, risk factors, and CMR parameters across 4 age categories (44–54, 55–64, 65–74, and 75–84 years), and \( \chi^2 \) tests were used to evaluate the differences across the same age categories for categorical variables. The Wilcoxon rank-sum test was used to test the different distributions of torsion levels between men and women.

Multivariable linear regression models were used to evaluate the effects of age, sex, and hypertension on the CMR measurements. Specifically, different CMR measurements (LV end-systolic volume and LVEDV, among others) were used as dependent variables, and the potential covariates include age, sex, ethnicity, heart rate, smoking, systolic BP, total cholesterol, glucose, glomerular filtration rate, and the use of medication to control hypertension, lipidemia, or diabetes mellitus, among others. For regression models with torsion and CS as dependent variables, LVEDV was included as a covariate in addition to the covariates used for other CMR measurements. To evaluate the relationship between LV measurements and gradations of BPs, the regression models included the same covariate adjustments with systolic BP excluded.

Standardized values were defined by dividing the differences between the observed values and the sample means by the corresponding standard deviations. Nonparametric regression estimates for the unknown curves were computed with the LOWESS smoothing method and the local linear smoothing method. The Epanechnikov kernel and a bandwidth of 8 were used for the local linear smoothing method. Statistical analyses were performed with the STATA statistical software package (version 11; Stata Corp, College Station, TX). A 2-sided value of \( P \leq 0.05 \) was considered statistically significant.

**Results**

The participants’ mean age was 65.0±9.7 years and 46.4% were women in the MESA baseline examination. Baseline characteristics according to age categories are displayed in Table 1. Systolic and pulse pressures were greater with increased age. Hypertension was more common among older participants. Of the total population, 14% were diabetic, 48% were hypertensive, and 48% had neither of these conditions.

**Torsion by Age Category and Sex**

The change in rotation from base to apex was approximately linear (Figure 1C), and the median distance from the basal to the apical slice was 3.0 cm (interquartile range, 3.0–3.01 cm). Overall, torsion was 3.9±1.3°/cm and differed significantly between women and men (4.2±1.3°/cm versus 3.5±1.1°/cm; \( P<0.001 \)). Torsion was found to differ by sex in all age categories (Figure 2).

**LV Structure and Function with Age, Sex, and Hypertension**

Associations of LV structure and function with age, sex, and hypertension in multivariable linear regression models are displayed in Table 2. Older age was associated with lower LV end-systolic volume, LVEDV, and SV and higher M/V ratio (−2.9, −6.5, and −3.6 mL per decade and 0.03 g/mL respectively; all \( P<0.001 \)). CS also was significantly lower with older age (−0.17% per decade; \( P<0.05 \)), and torsion was greater with older age (0.14°/cm per decade; \( P<0.001 \)) after adjustment for...
traditional risk factors. But the association of torsion with age was no longer significant after adjustment for LVEDV in addition to traditional risk factors. The T/SV ratio, which can be interpreted as torsion compensation for lower SV, and the T/CS ratio, interpreted as torsion relative to myocardial dysfunction, were significantly higher with older age.

LV end-systolic volume and LVEDV were lower in women (6.4 mL versus men, respectively; both \( P < 0.05 \)), but SV did not differ between sexes. The LV sphericity index and CS were higher in women (3.3% and 1.05% versus men, respectively; both \( P < 0.001 \)). In addition, torsion was greater in women (0.37°/cm versus men; \( P < 0.001 \)), and the sex differences remained highly significant after adjustment for LVEDV. There was significantly more torsion compensation (T/SV ratio) with lower SV in women (3.7°/cm \( L^{-1} \) versus men; \( P < 0.05 \)), but no differences in myocardial dysfunction (T/CS ratio) were documented.

Hypertensive participants had higher LV mass and M/V ratio (15.5 g and 0.07 g/mL, respectively; both \( P < 0.001 \)). CS was lower in hypertensive MESA participants (0.42%; \( P < 0.01 \)) and torsion was higher (0.17°/cm; \( P < 0.05 \)) compared with participants without hypertension. In hypertensive participants, greater myocardial dysfunction expressed by a greater T/CS ratio was observed, but there was no increase in the T/SV ratio.

The relation of LV structure and function with gradations of BPs is shown in Table 3. Higher systolic BP was associated with greater LVEDV (1.6 mL/10 mm Hg; \( P < 0.001 \)) and higher LV mass (3.2 g/10 mm Hg; \( P < 0.001 \)). Torsion correlated positively with systolic BP (0.06°/cm per 10 mm Hg; \( P < 0.05 \)) and pulse pressure (0.11°/cm per 10 mm Hg; \( P < 0.05 \)), but no correlation was found with diastolic BP. The associations of LV remodeling and torsion with increasing BP are displayed in Figure 3. The correlations between torsion and LV measurements are shown in Figure 4 and the influence of hypertension on torsion and age-related remodeling is displayed in Figure 5.

Reproducibility of LV Torsion
To assess interobserver and intraobserver variability, 30 cases were randomly selected and then independently analyzed by 2

---

**Table 1. Baseline Characteristics According to Age Categories**

<table>
<thead>
<tr>
<th>Age Categories (n=1478)</th>
<th>45–54 y (n=260)</th>
<th>55–64 y (n=355)</th>
<th>65–74 y (n=573)</th>
<th>75–84 y (n=290)</th>
<th>( P ) for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>49.9 (2.9)</td>
<td>59.5 (2.8)</td>
<td>68.8 (2.8)</td>
<td>78.0 (2.5)</td>
<td>...</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>71 (27.3)</td>
<td>104 (29.3)</td>
<td>171 (29.8)</td>
<td>93 (32.1)</td>
<td>0.021</td>
</tr>
<tr>
<td>Chinese American</td>
<td>24 (9.2)</td>
<td>49 (13.8)</td>
<td>94 (16.4)</td>
<td>41 (14.1)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>96 (36.9)</td>
<td>94 (26.5)</td>
<td>151 (26.3)</td>
<td>68 (23.5)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>69 (26.5)</td>
<td>108 (30.4)</td>
<td>157 (27.4)</td>
<td>88 (30.3)</td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>109 (41.9)</td>
<td>182 (51.3)</td>
<td>260 (45.4)</td>
<td>135 (46.6)</td>
<td>0.126</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169.2 (8.4)</td>
<td>165.9 (10.1)</td>
<td>165.3 (9.9)</td>
<td>163.7 (10.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.2 (5.0)</td>
<td>28.2 (4.8)</td>
<td>27.5 (4.6)</td>
<td>27.1 (4.6)</td>
<td>0.006</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>117.7 (16.1)</td>
<td>124.2 (18.6)</td>
<td>130.5 (21.3)</td>
<td>136.5 (21.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>73.1 (8.9)</td>
<td>72.9 (10.0)</td>
<td>71.9 (10.6)</td>
<td>69.6 (9.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>44.5 (10.4)</td>
<td>51.3 (13.7)</td>
<td>58.6 (16.8)</td>
<td>66.9 (18.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>61.9 (8.4)</td>
<td>63.8 (9.6)</td>
<td>62.3 (9.7)</td>
<td>61.8 (9.9)</td>
<td>0.180</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>61 (23.5)</td>
<td>142 (40.0)</td>
<td>321 (56.0)</td>
<td>181 (62.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>17 (6.5)</td>
<td>49 (13.8)</td>
<td>95 (16.6)</td>
<td>49 (17.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Smoker, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>124 (48.1)</td>
<td>187 (53.0)</td>
<td>287 (50.3)</td>
<td>168 (58.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Former</td>
<td>88 (34.1)</td>
<td>108 (30.6)</td>
<td>238 (41.7)</td>
<td>104 (36.1)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>46 (17.8)</td>
<td>58 (16.4)</td>
<td>46 (8.1)</td>
<td>16 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>195.2 (38.5)</td>
<td>198.7 (35.3)</td>
<td>193.8 (33.9)</td>
<td>190.6 (34.6)</td>
<td>0.025</td>
</tr>
<tr>
<td>GFR, mL/min</td>
<td>88.8 (14.3)</td>
<td>84.2 (17.3)</td>
<td>78.8 (17.5)</td>
<td>72.0 (17.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; GFR, glomerular filtration rate. Values are mean (SD).

Figure 2. Sex-specific torsion with age. Compared with people of younger ages, older women and men were more likely to have increased torsion (both tests for trends, \( P < 0.001 \)). Torsion differed significantly between women and men in each age category (all \( P < 0.001 \)). LV indicates left ventricular.
Table 3. Association of Left Ventricular Measurements With Gradation of Blood Pressure

<table>
<thead>
<tr>
<th>Coefficient (95% Confidence Interval)</th>
<th>Systolic BP, mm Hg</th>
<th>Diastolic BP, mm Hg</th>
<th>Pulse Pressure, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVESV, mL</td>
<td>0.4 (−0.01 to 0.8)</td>
<td>1.2 (0.4 to 2.0)</td>
<td>0.2 (−0.3 to 0.7)</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>1.6 (0.9 to 2.3)</td>
<td>1.5 (0.1 to 3.0)</td>
<td>2.3 (1.4 to 3.3)</td>
</tr>
<tr>
<td>SV, mL</td>
<td>1.2 (0.8 to 1.7)</td>
<td>0.4 (−0.6 to 1.3)</td>
<td>2.1 (1.5 to 2.7)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>0.1 (−0.1 to 0.3)</td>
<td>−0.6 (−0.9 to −0.2)</td>
<td>0.5 (0.2 to 0.8)</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>3.2 (2.4 to 4.0)</td>
<td>4.9 (3.3 to 6.6)</td>
<td>3.7 (2.6 to 4.8)</td>
</tr>
<tr>
<td>M/V ratio, g/mL</td>
<td>0.01 (0.003 to 0.02)</td>
<td>0.02 (0.01 to 0.04)</td>
<td>0.01 (−0.003 to 0.01)</td>
</tr>
<tr>
<td>LV sphericity index, %</td>
<td>0.02 (−0.15 to 0.18)</td>
<td>−0.12 (−0.45 to 0.21)</td>
<td>0.008 (−0.14 to 0.30)</td>
</tr>
<tr>
<td>Circumferential shortening, %</td>
<td>−0.06 (−0.13 to 0.00)</td>
<td>−0.29 (−0.43 to −0.15)</td>
<td>0.01 (−0.08 to 0.10)</td>
</tr>
<tr>
<td>Torsion, °/cm/cm−1</td>
<td>0.06 (0.03 to 0.10)</td>
<td>0.01 (−0.06 to 0.07)</td>
<td>0.11 (0.07 to 0.16)</td>
</tr>
<tr>
<td>T/CS ratio, °/cm per 1%</td>
<td>0.004 (0.003 to 0.01)</td>
<td>0.003 (−0.0005 to 0.007)</td>
<td>0.01 (0.004 to 0.01)</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; LVESV, left ventricular end-systolic volume; LVEDV, left ventricular end-diastolic volume; SV, stroke volume; LVEF, left ventricular ejection fraction; LV, left ventricular; M/V, mass/volume; T/SV, torsion/stroke volume; and T/CS, torsion/circumferential shortening. Coefficients represent change in dependent variables per 10-mm Hg increase in BP with adjustments for multiple variables: age, sex, ethnicity, height and heart rate, smoking, total cholesterol, glucose, glomerular filtration rate, and use of medication to control hypertension, lipemia, or diabetes mellitus.

*P<0.05.
†P<0.01.
‡P<0.001.

Discussion

Torsion is directly related to myocardial fiber orientation, structure, and function, and the assessment of torsion has been introduced as an important component of LV mechan-
ical behavior. The aim of the present study was to evaluate how LV remodeling associated with age, sex, and hypertension influences LV torsion in a large community-based population. In the present study, we demonstrate that torsion is higher with increased age and in women, that torsion is associated with lower LV volumes and circumferential strain, and that hypertension increases torsion independently of age and sex. Below, we first discuss the effects of age and sex on cardiac remodeling as a necessary prerequisite for a full understanding of the influence of hypertension on LV mechanical behavior.

Age and Torsion

It has been reported that LV twist is higher during infancy compared with adulthood. Torsion indexed to LV length, however, decreases until early adulthood because the LV elongates. Several small studies have suggested higher LV systolic wringing motion in older volunteers, as quantified by the twist magnitude measured by 2-dimensional speckle tracking echocardiography, circumferential to longitudinal shear angles measured by 3-dimensional tagged CMR, as well as torsion indexed to LV length with the use of Doppler tissue imaging. In the present study, we demonstrate that torsion is higher with increased age, and we found that this was related to a gradual increase in apical rather than basal rotation in a community-based population of individuals 45 to 84 years of age without history of cardiovascular diseases. Ageing has previously been associated with concentric remodeling, subendocardial dysfunction, and reduced elasticity of restoring forces of the LV, with consequent impaired LV recoil and untwist. The increase in peak systolic torsion appears to parallel the age-related progressive decline in subendocardial function, suggesting that reduced subendocardial function could result in less endocardial opposition to the dominant epicardium and thus enhanced torsion. Beyar and Sideman, using a theoretical mathematical model of LV mechanics, reported a shortening gradient across the LV wall with greater shortening in the subendocardial relative to the subepicardial myocardial layers when torsion was not considered in the model. In that analysis, the introduction of torsion reduced the need for endocardial myofiber shortening, with a consequent reduction in myocardial energy demand and oxygen consumption. The data suggest that torsion enables efficient LV systolic function without the need to augment endocardial shortening. In our study, the greater torsion seen in older participants could reflect a mechanism to compensate for lower myocardial shortening, with a consequent reduction in myocardial energy demand and oxygen consumption. In this regard, according to the lever-arm theory, a greater radius difference between the endocardium and the epicardium (ie, secondary to greater wall thickness relative to cavity radius) would result in increased torsion because helical contractions of the subendocardial and subepicardial muscle layers would counteract one another. With increasing age, LV volumes become smaller and the M/V ratio is greater with enhanced radius difference between endocardium and epicardium, lead-

Figure 3. Left ventricular (LV) remodeling and torsion with gradation of blood pressures (BPs). Systolic BP increased LV mass/height \(^{1.7} \) (A), mass/volume ratio (B), and torsion (C). Pulse pressure was associated with torsion (D). Red, green, and blue dots represent participants with medication for BP, all participants, and participants without medication for BP (n=873), respectively.
ing to enhanced torsion. However, in the present study, torsion was not positively correlated with M/V ratio, suggesting that a reduction in myocardial shortening rather than the pure effect of the lever-arm theory is responsible for the age-related increase in torsion. Indeed, previous studies from our group have reported that myofiber shortening is progressively lower in MESA participants with increased LV M/V ratio owing to the deleterious effects of concentric remodeling.33

Sex Differences in LV Torsion

In the present study, torsion and CS were higher in women compared with men. Several studies have shown that women have higher LV ejection fractions20,40 and greater systolic elastance than men, reflecting greater myocardial contractility.34 In the normal ventricle, the helical fiber orientation enables systolic fiber rearrangement, and during contraction, the subendocardial fibers are sheared toward the LV cavity, thus enhancing LV wall thickening.4,7 During LV ejection, LV twist has been shown to be linearly and negatively related to LV volume.41 In the present study, we demonstrate that peak torsion is negatively related to both end-systolic and end-diastolic LV volumes. Hearts with smaller ventricles exhibit greater torsion as proposed by the lever-arm theory (discussed previously in the Age and Torsion section). We also found that hypertensive individuals had a higher T/CS ratio without differences in the T/SV ratio. This pattern of concentric remodeling might enhance torsion because of the greater radius difference between the endocardium and the epicardium as proposed by the lever-arm theory (discussed previously in the Age and Torsion section). We also found that hypertensive individuals had a higher T/CS ratio without differences in the T/SV ratio. This pattern of concentric remodeling might enhance torsion because of the greater radius difference between the endocardium and the epicardium as proposed by the lever-arm theory (discussed previously in the Age and Torsion section).

Hypertension and Torsion

In the present study, we demonstrated that the hypertensive heart has higher LV mass and M/V ratio and that hypertension is an independent predictor of increased torsion. In pressure-overload hypertrophy, increasing systolic wall stress leads to increasing LV wall thickness as a compensatory mechanism to minimize wall stress.5 This pattern of concentric remodeling might enhance torsion because of the greater radius difference between the endocardium and the epicardium as proposed by the lever-arm theory (discussed previously in the Age and Torsion section). We also found that hypertensive individuals had a higher T/CS ratio without differences in the T/SV ratio. This suggests that enhanced torsion is not caused by reduced LV volumes and that the mechanisms of increased torsion associated with hypertension may thus be at least in part different from those seen in...
association with aging alone. In hypertension, reduced CS would also be expected to reduce torsion. A possible explanation is the increased afterload associated with hypertension. It has been reported that chronic afterload augmentation leads to increased torsion but reduced CS in patients with aortic stenosis.43 The apparent contradiction involving increased torsion despite reduced CS may be explained by increased endocardial myocardial oxygen consumption, as demonstrated in patients with increased arterial stiffening.44 Because the oblique fiber structures of the endocardium and epicardium are oriented in different directions, reduced subendocardial function may alter the balance between the opposing rotational forces and thus result in enhanced torsion. This may in fact represent a compensatory mechanism to maintain cardiac function in the face of increased afterload and/or vascular stiffness. Torsion has been found to be lower with increasing extent of transmural ischemia or infarction.45,46 Consequently, increased torsion in hypertensive hypertrophy can function as an early indicator of systolic myocardial dysfunction likely to be predominantly at the subendocardial level. However, as myocardial dysfunction progresses to involve the entire transmural extent of the LV wall, torsion decreases, as documented in advanced decompensated hypertrophic cardiac disease.

Limitations
Approximately 17% of participants were excluded because of technical issues related to data acquisition and analysis. Even though tagged CMR is currently the reference method for assessment of LV deformation, the limitations of CMR and tagging will benefit from further technical development.

The median distance from the apical to basal slice was only 3 cm. Thus, the slices were relatively close to each other, which may lead to underestimation of torsion. We did not assess longitudinal strain, and the spatial resolution of the tagging sequences used is also limited. Despite these technical limitations, this is still the largest myocardial MRI tagging study performed so far, allowing unique investigation of cardiac mechanics at the population level.

Conclusions
Torsion assessed by tagged CMR is greater with hypertension, with older age, and in women compared with men in a large cohort of individuals without evidence of prior cardiovascular disease. Age is associated with lower LV volumes and greater relative wall thickness and is accompanied by lower myocardial CS, whereas torsion increases with older age. The smaller LV volumes with greater contraction in women drive the greater torsion. Hypertension is associated with greater LV volumes and relative wall thickness and with lower CS. Torsion, however, is greater in hypertensive individuals independently of age and sex. Torsion may therefore represent a compensatory mechanism that maintains

Figure 5. The influence of hypertension on torsion and age-related remodeling. Age was inversely associated with left ventricular mass index (LVMI), positively associated with the mass/volume (M/V) ratio (A), and inversely associated with stroke volume (SV) and circumferential shortening (CS). However, torsion was positively correlated with age, along with left ventricular ejection fraction (LVEF; B). In hypertensive participants, remodeling was characterized primarily by an upward parallel shift compared with nonhypertensive participants. At any age, hypertensive participants had higher LVMI and M/V (C). Torsion was higher despite lower CS compared with participants without hypertension (D). SV was lower with age but was maintained to a larger degree in hypertensive individuals, indicating that increased torsion in part compensates for the reduced CS in individuals with hypertension (HT; E).
an adequate SV and cardiac output in the face of progressively reduced LV volumes and myocardial shortening associated with ageing and/or hypertension.

Acknowledgments
We thank the other investigators, staff, and participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org.

Sources of Funding
This research was supported by contracts N01-HC-95159 through N01-HC-95169 from the National Heart, Lung and Blood Institute.

Disclosures
Dr Gjesdal received support from the Fulbright Foundation, the Norwegian Medical Association, and the Norwegian Research Council.

References
27. Van Der Toorn A, Barenbrug P, Snoep G, Van Der Veen FH, Delhaas T, Fonseca CG, Doughty RN, Sharpe N. Age-related changes in myocardial deformation and twist using two-dimensional speckle-tracking echocardiography: an observational study using the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org.


CLINICAL PERSPECTIVE

Left ventricular (LV) systolic torsion limits myocardial energy consumption and minimizes transmural fiber stress gradients and oxygen demand, resulting in a more efficient contraction in the mathematical model. According to the lever-arm theory, a greater radius difference between the endocardium and the epicardium such as concentric hypertrophy would result in increased torsion. In addition, reduced subendocardial function would result in less opposition to the dominant epicardium and finally enhanced torsion because helical contraction of subendocardial and subepicardial muscle layers would counteract one another. However, the influence of LV remodeling associated with age, sex, and hypertension on LV torsion is not well understood. Therefore, we used cardiac magnetic resonance imaging to examine LV structure and function among 1478 participants of the Multi-Ethnic Study of Atherosclerosis who had no cardiovascular disease at baseline. In multivariable regression models, older age was associated with lower LV volumes, higher relative wall thickness, and a significant fall in stroke volume, along with lower myocardial shortening. However, torsion was greater with old age (0.14°/cm per decade; P<0.001). The smaller LV and higher contraction of women’s hearts were accompanied by the greater torsion (0.37°/cm versus men; P<0.001). Finally, although hypertension is associated with concentric hypertrophy and lower circumferential shortening, torsion is greater in hypertensive individuals independently of age and sex (0.17°/cm versus nonhypertension; P<0.05). These findings suggest that torsion represents a compensatory mechanism that maintains an adequate stroke volume and cardiac output in the face of progressively reduced LV volumes and myocardial shortening associated with ageing and/or hypertension.
Age, Sex, and Hypertension-Related Remodeling Influences Left Ventricular Torsion Assessed by Tagged Cardiac Magnetic Resonance in Asymptomatic Individuals: The Multi-Ethnic Study of Atherosclerosis
Kihei Yoneyama, Ola Gjesdal, Eui-Young Choi, Colin O. Wu, W. Gregory Hundley, Antoinette S. Gomes, Chia-Ying Liu, Robyn L. McClelland, David A. Bluemke and Joao A.C. Lima

Circulation. 2012;126:2481-2490; originally published online November 12, 2012; doi: 10.1161/CIRCULATIONAHA.112.093146
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/126/21/2481

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/