ORIGINAL RESEARCH

Left Ventricular Torsion Associated With Aortic Stiffness in Hypertension

Jean-Barthelemy Gnakamene, MD; Michel E. Safar, MD, PhD; Bernard I. Levy, MD, PhD; Brigitte Escoubet, MD, PhD

Background—Left ventricular (LV) torsion plays a key role in cardiac efficiency. In hypertension, aortic stiffening augments cardiac afterload. However, little is known about the links between LV regional contraction and aortic stiffness. We, therefore, investigated these relationships and their contribution to LV diastolic function.

Methods and Results—The study included normotensive and hypertensive individuals with normal LV ejection. Apical, basal, and global LV rotation rate and LV global longitudinal strain were measured (2-dimensional speckle tracking echocardiography). Aortic stiffness was calculated from carotid-femoral pulse wave velocity, and LV relaxation was calculated from early diastolic mitral annulus motion. The ratio of basal or apical untwist/twist rates was calculated to assess relationships between aortic stiffness and LV torsion parameters. LV twist and untwist rates were greater in hypertensive than normotensive individuals because of increased basal twist ($P<0.001$) and untwist ($P<0.001$) rates. LV relaxation was reduced (early diastolic mitral annulus motion=7.4±1.9 versus 10.4±2.3 cm/s; $P<0.001$). In the whole population, basal untwist rate increased with aortic stiffening ($R=0.43$; $P<0.001$) and LV relaxation ($R=0.41$; $P=0.001$). The ratio of basal untwist/twist rate was positively correlated with carotid-femoral pulse wave velocity, and in the hypertensive group, was greater than in the control group and positively correlated to carotid-femoral pulse wave velocity($P<0.001$). Results were independent of age, treatment, mean blood pressure, and indexed LV mass.

Conclusions—In hypertensive individuals, greater basal LV torsion was associated with increased aortic stiffness and improved diastolic function. These changes may compensate for the deleterious effects of aortic stiffening on LV relaxation. **(*J Am Heart Assoc*. 2018;7:e007427. DOI: 10.1161/JAHA.117.007427.)**

Key Words: aortic stiffness • hypertension • left ventricular torsion

Left ventricular (LV) motion can essentially be explained by the helical myocardial structure model described in the 1980s by Torrent-Guasp et al[1] and subsequently updated by Buckberg et al,[2] whereby a myocardial band links the pulmonary artery to the aorta through the LV apex. This model has been widely studied using magnetic resonance imaging[3,4] and echocardiographic speckle tracking imaging.[5–7] The LV torsion corresponds to an overall systolic twist, causing ejection of blood into the systemic circulation. This process is followed by a diastolic untwist that assists in LV filling. Furthermore, LV torsion is associated with the contraction of longitudinal and circumferential myocardial fibres.[8] In addition, magnetic resonance imaging studies have recently highlighted the role of myocardial laminar microstructures (sheetlets), which are reoriented during the cardiac cycle in a helical arrangement of the myocardium and may be the prevailing mechanism of LV motion.[9] During systole, until aortic valve closure, LV contraction prevails over the hemodynamic constraints of input impedance that characterize LV workload and is linked to arterial stiffness, arterial inertance, and peripheral resistance.[10] Carotid-femoral pulse wave velocity (CF-PWV) is an established marker of aortic stiffness,[11,12] and contributes to late afterload when increased incident PWV causes the reflected pulse wave to occur in late systole rather than in diastole after the aortic valve closure.[13,14] This finding has been reported in hypertensive

From the Department of Physiology, Hôpital Bichat (J.-B.G., B.E.), and Centre de Diagnostic et Thérapeutique Cardiovasculaire, Hôpital Hôtel-Dieu (J.-B.G., M.E.S.), Assistance Publique-Hôpitaux de Paris, Paris, France; Paris Descartes University, Paris, France (M.E.S.); INSERM U-970, Centre de Recherches Cardiovasculaire, Paris, France (B.L.); Vessels and Blood Institute, Hôpital Lariboisière, Paris, France (B.L.); Pôle de Recherche et d'Enseignement Supérieur Sorbonne Paris Cité, Paris Diderot University, Paris, France (B.E.); and INSERM U-1138, Centre de Recherche des Cordeliers, Paris, France (B.E.).

Correspondence to: Jean-Barthelemy Gnakamene, MD, Centre de Diagnostic et de Thérapeutique, Hôpital Hôtel-Dieu, 1 Place du Parvis Notre Dame, 75004 Paris, France. E-mail: jb.gnakamene@gmail.com

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Clinical Perspective

What Is New?

- Increased arterial stiffness is associated with changes in left ventricular (LV) torsion and corresponds to a change in cardiac mechanics that likely contributes to normal LV filling, despite LV hypertrophy and impaired relaxation in preserved ejection fraction.
- In the early stages of hypertensive disease, aortic stiffness (assessed by carotid-femoral pulse wave velocity) appears to be correlated with LV basal twist and untwist and cardiovascular risk.
- The changes in LV regional mechanics may be more strongly associated with the microcirculation or coronary perfusion than hemodynamic parameters.

What Are the Clinical Implications?

- The link between arterial stiffness and cardiac mechanics will pave the way toward a better understanding of diastolic heart failure.
- Age, sex, metabolic status, and hemodynamic constraints also have likely implications for the treatment of diastolic heart failure.
- In the near future, anti-ischemic and angiogenic therapies will likely have roles to play in the early stages of hypertensive disease.

subjects with increased CF-PWV.[15] There is, therefore, a strong correlation between CF-PWV and cardiovascular events and cardiovascular mortality.[12]

It is generally recognized that increases in aortic stiffness and, hence, in late afterload likely contribute to LV diastolic dysfunction and diastolic heart failure.[16,17] Moreover, in subjects with normal LV ejection fraction, LV torsion, and particularly the untwist component, plays a role in normal LV filling.[18,19] By studying healthy subjects from childhood to adulthood, Notomi et al[20] showed that basal twist velocity increases with age during childhood, whereas apical twist velocity remains unchanged. This process of differential increase in basal and apical twist velocity in childhood is specific to maturation. We hypothesize that, in adulthood, increased arterial stiffness and, thus, impaired arterial function may result in later changes in LV twist rates, possibly as an adaptive mechanism and related to LV basal rotation. The association between aortic stiffness and LV basal and apical twist and untwist rates has not previously been widely investigated in hypertensive disease. Therefore, in control and hypertensive adults with preserved LV ejection fraction, we measured the basal and apical systolic and diastolic rotation rates, a characteristic of diastolic relaxation evaluated by peak early diastolic mitral annulus velocity (E′), and CF-PWV as an index of arterial stiffness. Our study gave particular focus to possible links between aortic stiffness, LV basal and apical motions, and LV diastolic function.

Methods

The data, analytic methods, and study materials will not immediately be made available to other researchers for purposes of reproducing the results or replicating the procedure because our study population is currently being enlarged to enable further analyses and testing of novel hypotheses.

Study Population

We included 65 consecutive patients: 32 normotensive and 33 hypertensive individuals with essential hypertension and referred to the Multidisciplinary Physiology Department of Bichat Hospital (Paris, France) for echocardiography and assessment of arterial stiffness. All participants signed an informed consent form. However, because the study was conducted in the context of routine care, approval from an institutional review committee was not required. Hypertension was defined as systolic blood pressure (BP) ≥140 mm Hg and/or diastolic BP ≥90 mm Hg, measured after a 10-minute period of rest, or a personal history of treatment for hypertension. BP was measured on the right arm using an automatic device (Omron 907) enabling mean BP (MBP) and pulse pressure to be calculated. Exclusion criteria were secondary hypertension, diabetes mellitus (type 1or type 2, including personal history of the disease, antidiabetic treatment, or glycated hemoglobin >6%), hypercholesterolemia (history of hypercholesterolemia or cholesterol-lowering treatment), low estimated glomerular filtration rate, coronary artery disease, any treatment other than antihypertensive drugs, severe LV hypertrophy, valve disease (higher than grade 1/4), previous cardiac surgery, heart failure, stroke, peripheral vascular disease, severe respiratory failure, or pregnancy. Of the 33 hypertensive individuals, 24 were receiving antihypertensive drugs, as follows: diuretics (n=12), β-blockers (n=5), angiotensin 2 receptor blockers (n=22), and calcium channel blockers (n=13).

Echocardiography

Comprehensive echocardiography

Comprehensive echocardiography was conducted (M3S probe, Vivid 7; GE, Buc, France), including an M-mode echocardiogram to compute LV mass indexed to body area (LVMI)[21] and end diastolic relative wall thickness. LV ejection fraction was calculated using the biplane Simpson method. LV diastolic function[22] was assessed by mitral inflow E and A

waves, isovolumic relaxation time, and early diastolic velocity E′ at the septal and lateral mitral annulus as an indicator of LV relaxation;[23] the E/E′ ratio was, therefore, used as an indicator of LV filling pressure.[24]

Torsion and longitudinal strain assessment

LV rotation (or LV twist) was assessed from short-axis parasternal 2-dimensional views of basal (mitral valve) and apical rotation with cine loop displays (frame-rate range, 90–115 frames/s).[5,6,25] Offline measures were conducted with the EchoPac software (version 5) with semiautomatic border detection. LV angular displacement around the long axis was calculated as the average rotation of 6 segments obtained in basal, and 4 in apical, slices during systole and diastole. On rotation curves, after the offline tracking process, the peak was used as the maximal systolic rotation of the basal or apical LV region. Global LV rotation was automatically computed as apical minus basal LV rotations and also displayed as rotation curve during the cardiac cycle. We used the terms "rotation" or "twist" to designate the LV or LV basal or apical angle during systole around the longitudinal LV axis relative to the starting position, "untwist" to designate the angle during diastole relative to the systolic peak, and "LV torsion" for the resulting motion of apical and basal twists and untwists. By convention, counterclockwise rotation, as viewed from the apex, is expressed as a positive value; and clockwise rotation, as a negative value. LV twist results from counterclockwise rotation of the apex and clockwise rotation of the base, with the opposite occurring for LV untwist.[25]

Rotation (or twist) rate for basal, apical, and whole left ventricle was defined as the slope from the start of systole represented by the onset of QRS to the peak rotation on rotation curves; and untwist rate, as the slope from peak rotation to the rotation at mitral valve opening. They are expressed in degrees/s (°/s) (AB and BC in Figure 1A and 1B, respectively). To adjust for interindividual differences in heart rate, the time sequences were normalized to the percentage of systolic duration considered as 100% at aortic valve closure and with a value of 0% at the onset of QRS. All LV rotation values were derived from the averaging of 3 cycles.

LV global longitudinal strain (GLS) was obtained from apical 2-, 3-, and 4-chamber views on 17 segments corresponding to the basal, medium, and apical parts of the left ventricle. Systolic peak was detected on each strain curve after the offline tracking process and expressed as a percentage. The mean LV peak strain (GLS) and time to peak (TTP) were computed from all segment values. TTP strain was normalized as the percentage of systolic duration.

To determine the possible influence of CF-PWV on torsion parameters, the absolute ratio number of regional (apical or basal) untwist/twist rate (R regional u/t) was calculated. Correlations were then sought between this ratio and arterial function, or cardiac and clinical parameters in the whole population and in the control (normotensive) group (R1 regional u/t) or in the hypertensive group (R2 regional u/t).

CF-PWV measurement

CF-PWV was calculated from PW Doppler velocity of the right common carotid artery and the right common femoral artery (M10L probe).[12,26] To standardize the assessment of PWV, we measured the exact distance between the right common carotid artery and the right common femoral artery with a tape measure. We computed the transit time as the time difference between the onset of QRS and the intersecting tangent points of carotid and femoral Doppler waves. CF-PWV was calculated as the distance/time (m/s) ratio. Last, we used the scaling factor of 0.8 to convert the calculated CF-PWV into real CF-PWV values: CF-PWV=0.8×(distance$_{direct}$/time) m/s.[12]

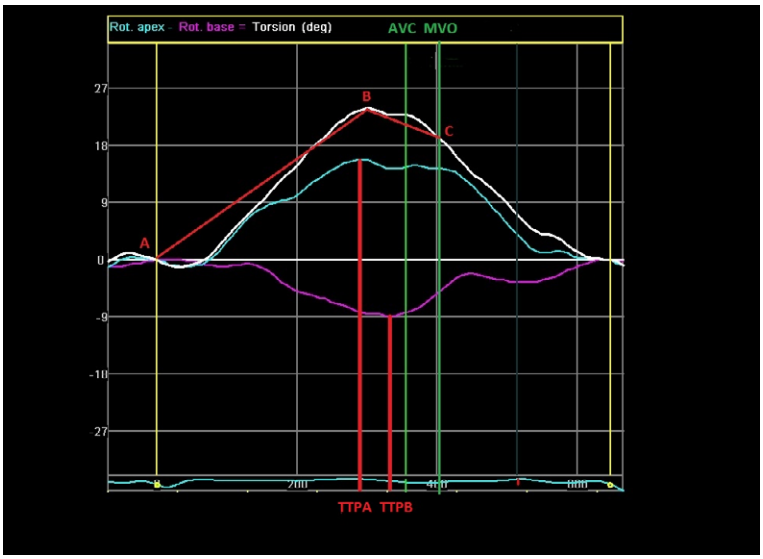
Statistical Analysis

Values are expressed as mean±SD and range. Statistical analyses were performed using NCSS 10 software (Version 10.0.11). Continuous variables were analyzed using 1-way ANOVA and Pearson's correlation coefficient. The χ^2 test was used to compare percentages, and Fisher's test was used to compare correlation coefficients. All correlation analyses were calculated in absolute numbers for the whole population (n=65). The R of basal u/t was also calculated separately for the control (n=32) and hypertensive (n=33) groups. Basal untwist rate and the ratio R of basal u/t rates were the outcome measures (dependent variables). Relationships between continuous variables were summarized by correlation coefficients derived from multiple regression analyses with and without adjustment for potential confounding variables (ie, age, treatment, MBP, LVMI, E′, GLS, and CF-PWV). We used the Bonferroni test to adjust the *P* values according to the number of comparisons and to establish the best regression model within the multiple regression analyses: α=0.05/number of comparisons. For the 1-way ANOVA, the χ^2 test, Fisher's test, and simple linear regression analysis, statistical significance was fixed at $P<0.05$.

Results

There were no differences between the control group and the hypertensive group in terms of age, sex, body mass index, heart rate, or LV ejection fraction (Table 1). In contrast, all 4 components of BP (systolic BP, diastolic BP, MBP, and pulse pressure) were higher in the hypertensive than in the control group. In comparison with the normotensive group, the hypertensive group exhibited evidence of LV

Normotensives



Hypertensives

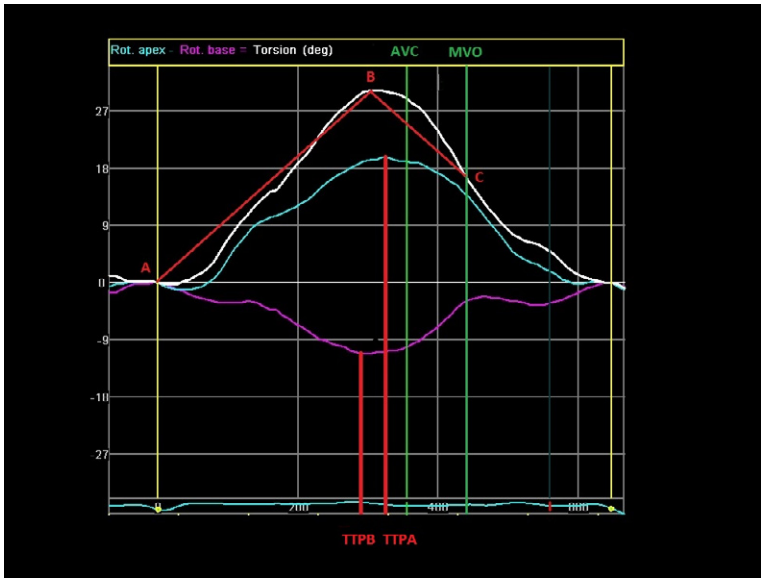


Figure 1. Examples of left ventricular (LV) rotation profile during the cardiac cycle in the normotensive and hypertensive groups. There were greater LV twist and untwist rates in the hypertensive group compared with the normotensive group. There was earlier apical than basal peak in the normotensive group, with the opposite occurring in the hypertensive group, possibly to compensate for the delayed apical peak. This suggests adaptation of both magnitude and timing for basal twist and untwist in the hypertensive group. A indicates LV rotation at onset of QRS; AB, twist rate; AVC, aortic valve closure; B, LV rotation at peak rotation; BC, untwist rate; C, LV rotation at mitral valve opening (MVO); Rot. apex, apical rotation (blue line); Rot. base, basal rotation (purple line); Torsion, LV torsion (white line); TTPA, time to peak (apical); and TTPB, time to peak (basal).

hypertrophy and concentric remodeling (greater LVMI and relative wall thickness), lower LV GLS with unchanged time to peak, a greater isovolumetric relaxation time, and diastolic dysfunction with lower E′ and E/A ratio and higher E/E′. Aortic stiffness (ascertained from CF-PWV) was also greater in the hypertensive than the normotensive group.

Table 1. Clinical and Echocardiographic Features of the Population

Features	Normotensive Group (n=32)		Hypertensive Group (n=33)		*P* Value
	Mean (SD)	Range	Mean (SD)	Range	
Age, y	50 (12)	28 to 73	54 (12)	32 to 76	0.372
Sex (male=0/female=1), %	0.61		0.57		0.774
BMI, kg/m²	26 (7)	17 to 52	28 (6)	17 to 54	0.457
Body height, cm	167 (10)	148 to 182	168 (10)	147 to 199	0.545
SBP, mm Hg	121 (15)	93 to 187	144 (20)	94 to 198	<0.001
DBP, mm Hg	72 (8)	52 to 92	82 (12)	54 to 108	<0.001
MBP, mm Hg	90 (10)	65 to 128	103 (13)	68 to 132	<0.001
PP, mm Hg	49 (10)	28 to 98	62 (16)	32 to 105	0.003
HR, beats/min	74 (8)	52 to 93	72 (9)	50 to 90	0.353
EF, %	63 (4)	55 to 77	61 (5)	52 to 73	0.245
Peak GLS, %	−19.9 (2)	−15.2 to −23	−17.5 (3)	−16.1 to −25.1	0.005
TTP GLS/Sys Dur, %	94 (4)	82 to 98	93 (3)	85 to 97	0.541
LVMI, g/m²	76 (17)	47 to 148	90 (19)	52 to 152	0.003
RWT	0.37 (0.05)	0.28 to 0.48	0.42 (0.04)	0.31 to 0.5	0.002
E, cm/s	82 (15)	51 to 121	75 (13)	51 to 106	0.071
E/A	1.37 (0.35)	0.3 to 2.1	0.95 (0.29)	0.28 to 1.8	<0.001
E′, cm/s	10.4 (2.3)	7 to 15.1	7.4 (1.9)	5 to 14.9	<0.001
E/E′	8.3 (2.2)	4.5 to 12.2	9.9 (2.1)	4.6 to 14.2	0.003
IVRT, ms	60 (18)	40 to 85	73 (18)	41 to 96	0.003
CF-PWV, m/s	8.1 (1.7)	5.3 to 12.6	11 (2.5)	5.7 to 16.6	<0.001

BMI indicates body mass index; CF-PWV, carotid-femoral pulse wave velocity; DBP, diastolic blood pressure; E, early mitral inflow; E/A, ratio of left ventricular (LV) filling with A as maximal velocity of auricular flow; E/E′, computed as an estimate of diastolic preauricular LV pressure (EDLVP; where a value of ≥15 was considered as EDLVP >12 mm Hg, and a value of ≤8 as EDLVP <12 mm Hg, with E as maximal velocity of rapid LV filling); E′, early diastolic maximal velocity of mitral annulus; EF, ejection fraction; GLS, global longitudinal strain; HR, heart rate; IVRT, isovolumetric relaxation time; LVMI, left ventricular mass indexed to body area; MBP, mean blood pressure; PP, pulse pressure; RWT, relative wall thickness (corresponding to the sum of posterior and septal wall thickness/the internal LV diameter, as an index of concentric LV hypertrophy); SBP, systolic blood pressure; Sys Dur, time to aortic valve closure; and TTP, time to peak.

Comparisons of mean CF-PWV and LV twist and untwist rates in the 3 groups (ie, control [n=32], untreated [n=9], and treated hypertensive [n=24] individuals) showed significant differences between both treated and untreated hypertensive subjects on one hand, and the control group on the other hand. There were, however, no significant differences between treated and untreated hypertensive subjects (Table 2).

LV Torsion in Hypertensive Subjects

LV peak rotation and twist and untwist rates were greater in hypertensive than in normotensive subjects, mainly because of greater LV basal peak rotation and twist and untwist rates (Table 3). Basal LV rotation TTP was shorter, and apical rotation TTP was longer, in the hypertensive group compared with the normotensive group. No correlation was found between LV torsion parameters and BP. A positive correlation was observed between LV basal twist and untwist rate absolute numbers (R=0.62; P<0.001) (Figure 2).

Associations Between LV Torsion, CF-PWV, and Diastolic Function

Correlation analysis of the whole population showed that LV twist and untwist rates were associated with increased aortic stiffness (CF-PWV) (Table 4). A strong association with CF-PWV was found for LV basal twist and untwist rates (Figure 3A and 3B), whereas the correlation with LV apical twist and untwist rates was not significant (Figure 3C and 3D); we did, however, observe a trend toward a significant correlation between increasing CF-PWV and decreasing apical untwist rate. Correlation was also observed between CF-PWV and LV or LV basal peak rotation (R=0.40 [P=0.001] or R=0.43 [P<0.001], respectively). LV and LV basal and apical twist rates increased with increasing LV mass and concentric remodeling (relative wall

Table 2. Comparisons Between Control, Untreated, and Treated Hypertensive Groups

Variable	Control Group (n=32)	*P* Value (Between Control and Untreated Hypertensive Groups)	Untreated Hypertensive Group (n=9)	*P* Value (Between Untreated and Treated Hypertensive Groups)	Treated Hypertensive Group (n=24)
CF-PWV, m/s	8.1 (1.7)	<0.001	11.6 (2.7)	0.452	10.8 (2.8)
LV twist, °/s	67.4 (12.6)	0.003	72.5 (8.2)	0.562	73.8 (15.3)
LV untwist, °/s	−67.7 (22.3)	0.008	−79.5 (23.1)	0.223	−85.9 (22.2)

Data are given as mean (SD). CF-PWV indicates carotid-femoral pulse wave velocity; and LV, left ventricular.

thickness) (Table 4). LV and LV basal and apical untwist rates increased with improved diastolic parameters (E′ and E/E′) (Figure 4, Table 4). LV basal twist rates increased with decreasing longitudinal LV systolic function, as assessed by GLS (Figure 5, Table 4). CF-PWV increased with abnormal diastolic parameters E′ (R=−0.53; P<0.001) and E/E′ (R=0.38; P=0.004) and with decreased GLS (R=−0.43; P<0.001). After normalization to systolic duration, apical time to peak was delayed with increasing CF-PWV (R=0.371; P=0.003) (Figure 6A), whereas in contrast, basal time to peak was earlier (R=−0.354; P=0.005) (Figure 6B). In multiple linear regression analysis, basal untwist rate was positively associated with CF-PWV and E′, independently of age, treatment, MBP, LVMI, and GLS (Table 5). The ratio R of basal u/t was greater in the hypertensive than in the control group (Table 3), and in the whole population was positively associated with CF-PWV (R=0.61; P<0.001) (Figure 7A) and E′ (R=0.45; P<0.001). In the hypertensive group, a positive correlation was also observed between the ratio R2 of basal u/t and CF-PWV (R2=0.53; P=0.002), whereas no correlation was found with the control group (R1=0.11; P=0.587) (Figure 7B). There was no significant correlation between the R of apical u/t and CF-PWV in either the whole population or the control or hypertensive groups. Last, in multiple linear regression analysis, the ratio R of basal u/t was positively associated with CF-PWV and E′, independently of age, treatment, MBP, LVMI, and GLS (Table 6).

Table 3. LV Torsion

Variable	Normotensive Group (n=32)	Hypertensive Group (n=33)	*P* Value
Apical			
Peak rotation, °	9.6 (4.1)	11 (4.3)	0.211
Time to peak/Sys Dur, %	88	96	0.005
Twist rate, °/s	42.7 (14.4)	44.2 (12.3)	0.754
Untwist rate, °/s	−43.7 (11.5)	−42.2 (10.4)	0.724
Basal			
Peak rotation, °	−6 (1.8)	−8.4 (3.3)	0.002
Time to peak/Sys Dur, %	97	87	<0.001
Twist rate, °/s	−29.2 (6.3)	−36.8 (8.6)	<0.001
Untwist rate, °/s	32.6 (9.4)	43.9 (12.9)	<0.001
LV			
Peak rotation, °	14.4 (5)	17.6 (5.7)	0.001
Time to peak/Sys Dur, %	95	92	0.452
Twist rate, °/s	67.4 (12.6)	73.5 (13.2)	0.005
Untwist rate, °/s	−67.7 (22.6)	−84.2 (22.4)	0.001
R apical u/t, %	102	97	0.071
R basal u/t, %	111	120	0.006

Data are given as mean (SD). LV indicates left ventricular; R apical u/t, ratio of apical untwist/twist rate; R basal u/t, ratio of basal untwist/twist rate; and Sys Dur, time to aortic valve closure.

Discussion

The main findings of this study are as follows: (1) LV torsion rate was greater in hypertensive subjects than in normotensive controls, because of greater basal twist and untwist rates with no significant changes in apical twist and untwist rates; (2) in the whole population, greater LV and LV basal twist and untwist rates were positively associated with aortic stiffness;

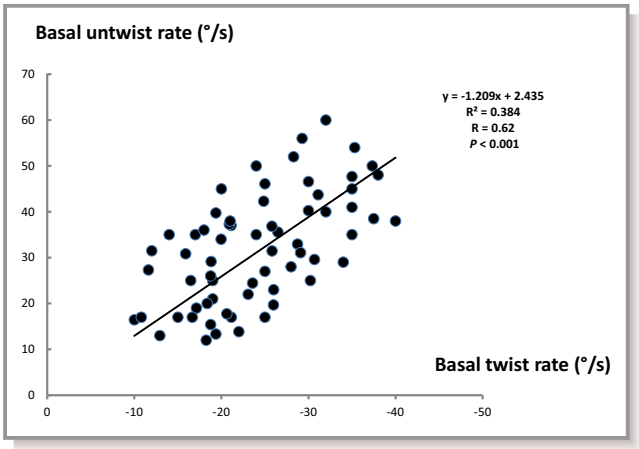


Figure 2. Overall population: correlation between basal twist and untwist rates (N=65).

Table 4. Overall Study Population: Correlation of Torsion and Arterial Stiffness, Clinical, and Cardiac Parameters (With All Parameters in Absolute Numbers)

Clinical and Cardiac Parameters (N=65)	Apical				Basal				LV			
	Twist, °/s		Untwist, °/s		Twist, °/s		Untwist, °/s		Twist, °/s		Untwist, °/s	
	R	*P* Value	*R*	*P* Value	*R*	*P* Value	*R*	*P* Value	*R*	*P* Value	*R*	*P* Value
CF-PWV, m/s	−0.17	0.311	−0.33	0.081	0.42	<0.001	0.43	<0.001	0.40	0.001	0.42	<0.001
LVMI, g/m^2	0.39	0.002	0.30	0.092	0.42	<0.001	0.2	0.174	0.4	0.004	0.12	0.423
RWT	0.38	0.005	0.1	0.461	0.39	0.005	0.11	0.421	0.38	0.005	0.18	0.163
GLS, %	−0.2	0.123	0.14	0.421	−0.41	0.001	−0.32	0.187	−0.21	0.144	−0.25	0.311
E′, cm/s	0.3	0.154	0.38	0.006	0.34	0.083	0.41	0.001	0.22	0.154	0.4	0.001
E/E′	−0.12	0.423	−0.37	0.011	−0.32	0.183	−0.38	0.004	−0.25	0.127	−0.37	0.008

CF-PWV indicates carotid-femoral pulse wave velocity; E, maximal velocity of early LV filling; E/E′, ratio used as estimation of LV filling pressure; E′, early diastolic maximal velocity of mitral annulus; GLS, global longitudinal strain; LV, left ventricular; LVMI, LV mass indexed to body area; RWT, relative wall thickness (as the sum of posterior and septal wall thickness in diastole/the internal LV diastolic diameter).

and (3) greater CF-PWV and lower LV basal untwist were associated with impaired LV diastolic function.

LV Torsion in Hypertension

Because cardiac hypertrophy is commonly observed in hypertension, the role of LVMI changes in LV adaptive mechanisms merits discussion. We observed that concentric hypertrophy was associated with increasing LV and LV apical and basal twist rates. LV torsion results from the cocontraction of overlapped subepicardial and subendocardial myocardial layers that are orthogonally oriented in a helical myocardial structure, thus causing rotation of the apex and the base in opposite directions.[5–7] External subepicardial layers with a larger radius of curvature than subendocardial layers ensure the predominant direction of LV rotation.[27] Thus, in LV concentric hypertrophy, subepicardial layers are more widely expressed as force and lead to greater LV rotation than in nonhypertrophic LV hypertrophy, as was observed in our study. A positive association between LV mass and LV torsion was also observed by Park et al[28] in a group of hypertensive patients with LV hypertrophy and mild diastolic dysfunction. In contrast, LV torsion was normalized or reduced in advanced diastolic dysfunction with increased filling pressure, suggesting that changes in torsion may contribute to LV adaptation in early stages of hypertensive cardiomyopathy. Our observations of increased LV twist and untwist rates in mild hypertensive disease[29] were consistent with this finding.

In addition, the increased torsion may be secondary to subendocardial dysfunction, as described in ischemia,[30] and to the decrease in myocardial capillary density (rarefaction) associated with hypertension.[31–33] This may result in greater functional involvement of the subepicardial layers contributing to increased LV torsion,[1] with unequal contraction of the subendocardial layers that are more sensitive to ischemia.

LV Torsion and Aortic Stiffness

We found a positive correlation between CF-PWV and LV basal twist or untwist rates (Figure 3A or 3B) or peak rotation as well as with these torsional parameters for the whole left ventricle, whereas no significant correlation was observed with LV apical rotation parameters.

The association between LV torsion and CF-PWV may reflect a systolic constraint in LV twist, during the rapid ejection phase (or early systole), opposing the inertial and capacitive properties of the arterial tree, and the early LV untwist, beginning during the late ejection phase (or late systole), notably characterized by the possible occurrence of reflected aortic waves.[34] Greater aortic stiffness results in increased pulse pressure and incident pulse wave and, thus, increased and faster reflected waves occurring during late systole rather than in diastole. Together, these factors contribute to increased afterload,[17,18] increased oxygen demand, and lower diastolic coronary perfusion pressure, which can lead to myocardial ischemia and thus increased LV torsion.

As shown by Shin et al[35] in hypertensive patients with normal ejection fraction, an increase in ventricular-arterial coupling, as assessed by the ratio of arterial/LV end systolic elastance, is associated with increased LV twist. The authors suggested this may be a compensatory mechanism related to LV changes in systolic function in the early stages of LV hypertrophy. In line with these findings, we observed an increasing basal twist rate with increasing LVMI and showed that LV basal twist rate was associated with increased arterial stiffness and with decreased longitudinal LV deformation

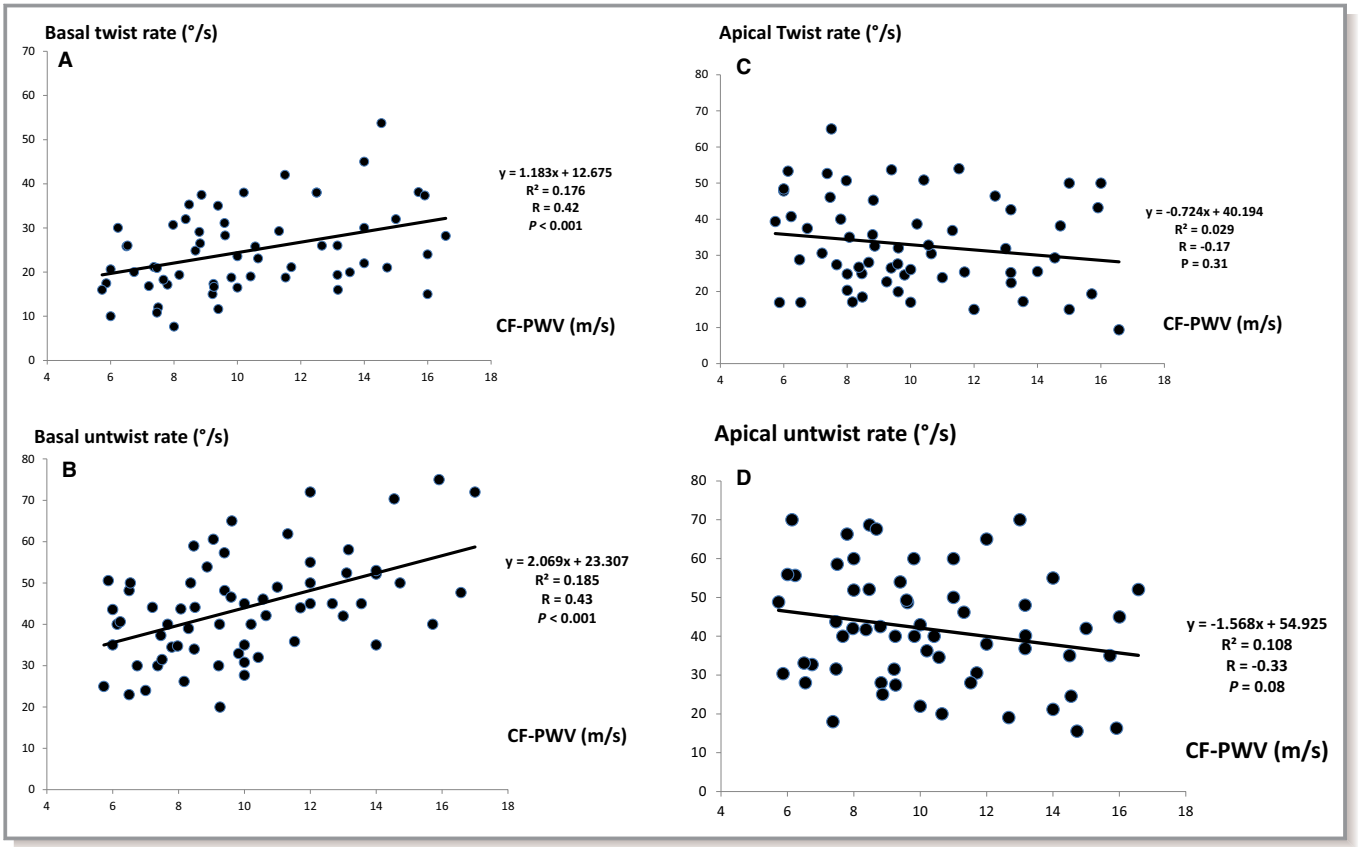


Figure 3. A, Overall population (N=65): correlation between left ventricular basal twist rate and aortic stiffness. B, Overall population (N=65): correlation between left ventricular basal untwist rate and aortic stiffness. C, Overall population (N=65): correlation between left ventricular apical twist rate and aortic stiffness. D, Overall population (N=65): correlation between left ventricular apical untwist rate and aortic stiffness. CF-PWV indicates carotid-femoral pulse wave velocity.

(GLS) (Figure 5). This suggests the existence of a compensatory mechanism of basal LV twist despite increased aortic stiffness in the early stages of hypertensive cardiomyopathy.

Increases in LV torsion with increased aortic stiffness have been reported by Sulemane et al,[36] but this finding was limited to subjects with chronic kidney disease. In contrast, in untreated hypertensive individuals, Hwang et al[37] showed a negative correlation between arterial stiffness and peak LV basal rotation. These authors, however, used brachial-ankle PWV, which, unlike CF-PWV, is not a validated marker of

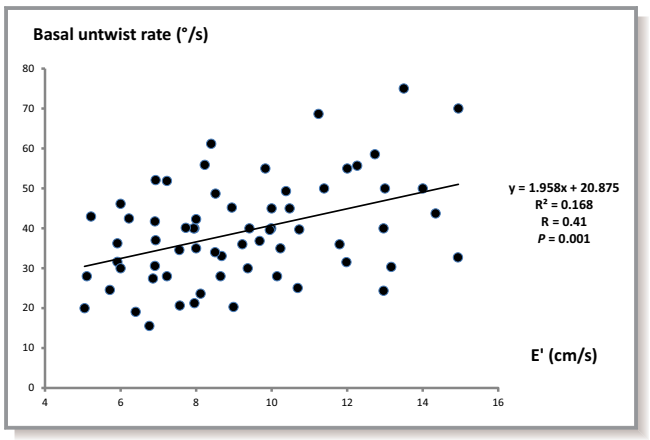


Figure 4. Overall population (N=65): correlation between left ventricular basal untwist rate and left ventricular diastolic function. E′ indicates early diastolic velocity of mitral annulus.

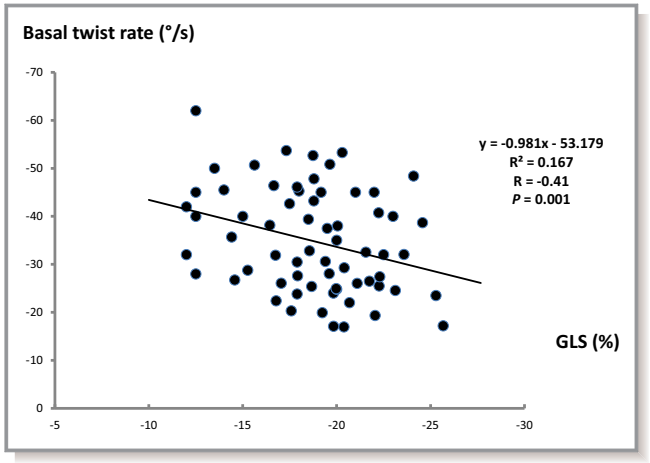


Figure 5. Overall population (N=65): relationship between left ventricular basal twist rate and global longitudinal left ventricular systolic function. GLS indicates global longitudinal strain.

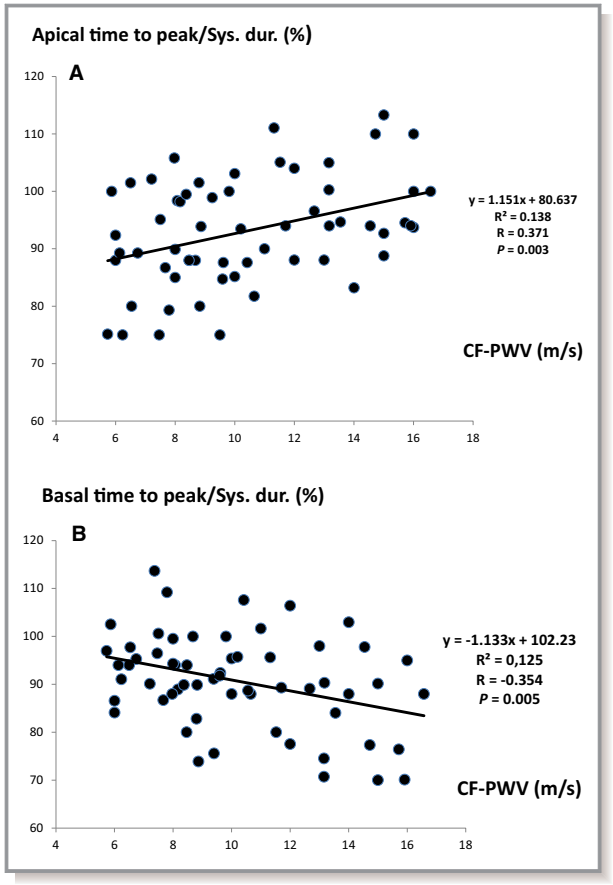


Figure 6. A, Overall population (N=65): relationship between left ventricular apical time to peak normalized and aortic stiffness. B, Overall population (N=65): relationship between left ventricular basal time to peak normalized and aortic stiffness. CF-PWV indicates carotid-femoral pulse wave velocity.

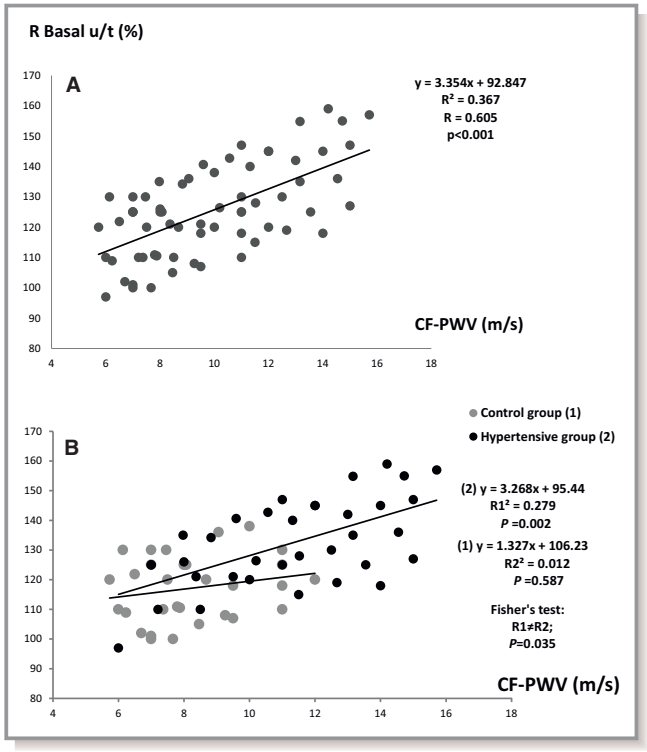


Figure 7. A, Correlation between the ratio of basal untwist rate/aortic stiffness in the whole study population (N=65). B, Correlations between the ratio of basal untwist to twist rate/aortic stiffness in the control and hypertensive groups. CF-PWV indicates carotid-femoral pulse wave velocity; R Basal u/t, ratio of basal untwist/twist rate; R1, ratio R of Basal u/t in control group (n=32); R2, ratio R of Basal u/t in hypertensive group (n=33).

cardiovascular risk[38,39] and does not explain the direct relationship between the LV and the aorta. In a large population of untreated hypertensive subjects, Ikonomidis et al[40] observed impaired LV untwisting associated with increased CF-PWV. However, unlike our study, which included both control and hypertensive individuals and thus considered hypertension as a continuing variable in the whole population,

Table 5. Multiple Linear Regression Analysis With Basal Untwist Rate as the Dependent Variable

Variable (N=65)	Regression Coefficient	R^2	*P* Value
Intercept	−25.72	···	0.432
Age, y	−0.09	0.035	0.231
Treatment (n=24)	9.41	0.001	0.654
MBP, mm Hg	0.12	0.004	0.092
LVMI, g/m^2	0.27	0.002	0.491
E′, m/s	3.23	0.101	0.004
GLS, %	−0.06	0.006	0.542
CF-PWV, m/s	3.77	0.159	0.001

Threshold of significance, *P*=0.007. CF-PWV indicates carotid-femoral pulse wave velocity; E′, early diastolic velocity of mitral annulus; GLS, global longitudinal strain; LVMI, left ventricular mass indexed to body area; and MBP, mean blood pressure.

Table 6. Multiple Linear Regression Analysis With the Ratio of Basal Untwist Rate/Twist Rate as the Dependent Variable

Variable (N=65)	Regression Coefficient	R^2	*P* Value
Intercept	101.66	···	0.122
Age, y	0.187	0.015	0.431
Treatment (n=24)	22.91	0.004	0.553
MBP, mm Hg	0.18	0.022	0.167
LVMI, g/m^2	0.253	0.005	0.421
E′, cm/s	62.45	0.097	0.006
GLS, %	0.01	0.002	0.674
CF-PWV, m/s	53.76	0.168	0.003

Threshold of significance, *P*=0.007. CF-PWV indicates carotid-femoral pulse wave velocity; E′, early diastolic velocity of mitral annulus; GLS, global longitudinal strain; LVMI, left ventricular mass indexed to body area; and MBP, mean blood pressure.

these contradictory observations to our own were limited to a hypertensive population. Last, in a cross-sectional multiethnic study, Ohyama et al[41] used magnetic resonance imaging to demonstrate that increased PWV was associated with reduced LV torsion. However, because the mean age of this population (69.5±9.4 years) was considerably higher than that of our study participants, potential differences in cardiac mechanics must also be taken into consideration.

The respective roles of the apex and the base in LV torsion during systole and diastole have not as yet been fully understood. By observing healthy subjects from childhood to adulthood, Notomi et al[20] observed a significant increase in basal rotation velocity during childhood, related to the maturational process of the LV twist-untwist motion, in contrast with a significant increase in apical rotation velocity in adulthood, related to increases in hemodynamic constraints. Again in healthy subjects, Kim et al[5] reported a gradual increase in LV basal rotation with increasing age that may play a role in maintaining systolic function. This could account for the differential impacts of fibrosis and ischemia on the regional LV myocardium,[1,42] or changes in electrical activation[43] with relatively well-preserved LV basal versus apical rotation.

Increased apical twist has typically been observed in severe LV pressure overload and in aortic stenosis, and it is considered to be an adaptive or compensatory mechanism.[44] Such pressure conditions are likely not yet present in the early stages of hypertensive cardiomyopathy, thus explaining the unchanged apical twist in both our groups. In contrast to apical twist, basal twist is not limited by the overlapping layers of the subendocardium (or descending myocardial segment from the LV base to apex) and the subepicardium (or ascending myocardial segment from the LV apex to base) that ensure the rotation of the apex as a torque of forces.[1,2] Thus, subepicardial ascending myocardial segment contraction related to basal twist and following descending myocardial segment contraction is not countered in the upper septum and the lateral free LV wall, notably in LV hypertrophy, which likely contributes to greater adaptive potential than apical torsion did in our study.

The ratio of basal untwist/twist rate was greater in hypertensive than in nonhypertensive control individuals (Table 3) and increased with increasing CF-PWV in the whole population (Figure 7A) as well as with E′, independently of age, treatment, MBP, LVMI, and GLS (Table 6). Moreover, in the hypertensive group (group 2), a positive association between CF-PWV and the ratio R2 of basal u/t was also observed, whereas no correlation was found in the control group (group 1) with the R1 of basal u/t (Figure 7B). To the best of our knowledge, this is the first time these features have been investigated. Our findings suggest a regional adaptive mechanism of untwist to twist rate in favor of the LV relaxation, associated with increased aortic stiffness and the presence of hypertension, whereas the latter is considered as a continuing variable in the whole population. No association was found between the ratio R of basal u/t and hemodynamic parameters in the whole population. Further investigations are needed to determine the exact mechanisms of this adaptation.

Aortic Stiffness, LV Torsion, and Diastolic Function

In the current study, parameters of LV diastolic function were seen to be impaired, lower (for E′) and higher (for E/E′ ratio), with higher CF-PWV and, conversely, with increased LV basal untwist rates (Figure 4). In addition, the positive associations between basal untwist rate and CF-PWV or E′ were independent of age, treatment, MBP, LVMI, and GLS (Table 5). Long-term increases in arterial stiffness, such as are observed in hypertension, are thought to lower and delay LV relaxation.[45] These impairments may be the result of early aortic wave reflections, as previously shown,[15] in hypertensive subjects with normal ejection fraction, or of changes in LV stiffness during late systole or early diastole.[46]

One of the main theories put forward to explain the mechanisms behind the diastolic LV untwist is that part of the energy stored during systole is produced during diastole as a recoil effect.[18,47] This contributes to the diastolic intraventricular pressure gradient that pulls the blood into the left ventricle in early diastole.[48] The increase in LV untwist rates may be closely related to increased LV twist rates, as suggested by the strong correlation that we observed between these 2 components of torsion (Figure 2). Thus, the association between increased aortic stiffness and LV twist and untwist rates likely reflects increased LV torsion that compensates for the deleterious effect of aortic stiffness on diastolic function in the early stages of hypertensive cardiomyopathy.

The diastolic untwist may well be a continuing process of systole in myocardial band contraction.[1,2] This possibly actively promotes the untwisting motion and changes in LV shape, such as the widening in diastole, that are related to the helical structure of the heart. In the hypertensive group of our study, we observed lower GLS[49,50] (Table 1) and increased LV basal rotation rate (Table 3), both associated with increased CF-PWV (Table 4). This suggests that an increased basal rotation rate may be an active compensatory mechanism to limit the deleterious effects of increased aortic stiffness on LV relaxation.

Furthermore, and in line with the observations we made in our control group (Table 3, Figure 1A), previous studies in healthy subjects have also shown that the LV apex rotates earlier than the LV base, thus creating the main LV torsional profile.[48] However, in our hypertensive group, we observed

delayed apical peak torsion and a trend toward a decreasing apical untwist rate with increased CF-PWV (Figure 6A and 6B), whereas the latter was associated with earlier basal peak torsion (Figure 6B) and greater basal untwist rate (Figure 3B). LV TTP remained unchanged (Table 3). These results suggest a temporal adaptation of the LV base to compensate for the delayed apical rotation (Figure 1A and 1B), which may represent the constraint of CF-PWV to apical untwist and the basal twist and untwist adaptation, not only in magnitude but also in time. This adaptation likely enables the onset of LV untwisting to coincide with the onset of LV relaxation that precedes and assists in LV filling.[18]

Limitations

Longitudinal studies to further investigate the links between cardiovascular risk and twist changes are required to confirm the findings of this cross-sectional study. We did not assess all components of LV contraction, such as the radial, circumferential, subendocardial, and subepicardial strain, which may play a role in the compensatory processes associated with impaired LV relaxation. Magnetic resonance imaging has recently been used to study different concepts of cardiac contraction (notably, the orientation of myocardial sheetlets)[9] and will likely improve our understanding of LV torsion. In our study, hemodynamic parameters were not assessed invasively and 24-hour ambulatory BP monitoring was not conducted, whereas this technique is useful for identifying the dipper/nondipper hypertensive profile and its consequences on LV mechanics. Indeed, Tadic et al used this technique to show that BP increases with LV torsion independently of the other risk factors.[51] The role of hypertrophy was limited to the LV concentric pattern and did not consider other forms, such as simple remodeling or eccentric hypertrophy, in the hypertensive disease.[52] Elevated fasting glucose and glycated hemoglobin have previously been shown to be associated with an increase in LV untwisting rate in normotensive subjects.[53] Findings such as this suggest that various risk factors may exert similar effects on the LV diastolic untwist that we considered as an adaptive mechanism in our study to avoid the increase in LV filling. However, the question of the limit and the mechanism of action of this possible adaptation, the role of the other risk factors, and the influence of sex[41] all warrant further investigation. Nagel et al[44] reported the particular case of aortic valve stenosis with preserved ejection fraction; in contrast to our own observations, they demonstrated low basal and high apical LV torsion. However, the presence of valvular plane calcification can limit LV basal adaptation. Interestingly, in this valvular disease, Sandstede et al[54] did not find any correlation between invasive BP measurements and torsion parameters, in line with our finding with the BP, thus suggesting that mechanical or other parameters may have a greater impact on myocardial wall function than LV pressure determinants. This may well add even greater potential to our findings.

Conclusion

The mechanical relationships between LV regional contraction and aortic stiffness have not been widely investigated, despite their established role in the onset of diastolic impairment and heart failure. Arterial stiffness is one of the main constraints opposing LV contraction in systole but also relaxation in diastole, thus highlighting the importance of an in-depth knowledge of the entire cardiovascular system, including at the least both the heart and the aorta. In our study population, we found an association between basal twist and untwist and increased aortic stiffness that likely plays an important role in preserving diastolic function in the early stages of hypertensive disease and potentially disappears in older subjects. This theory is corroborated by an in-depth understanding of myocardial contraction, particularly with regard to the helical anatomy and torsional function. Further investigations are required to document the changes in regional contraction and their relation with impaired arterial function in terms of age, sex, fibrosis, and the ischemic process. Future studies could also help to identify the most appropriate treatment strategy.

Disclosures

None.

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