Age-related changes in the biomechanics of left ventricular twist measured by speckle tracking echocardiography

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van Dalen BM, Soliman OI, Vletter WB, ten Cate FJ, Geleijnse ML. Age-related changes in the biomechanics of left ventricular twist measured by speckle tracking echocardiography. Am J Physiol Heart Circ Physiol 295: H1705–H1711, 2008. First published August 22, 2008; doi:10.1152/ajpheart.00513.2008.—The increasing number and proportion of aged individuals in the population warrants knowledge of normal physiological changes of left ventricular (LV) biomechanics with advancing age. LV twist describes the instantaneous circumferential motion of the apex with respect to the base of the heart and has an important role in LV ejection and filling. This study sought to investigate the biomechanics behind age-related changes in LV twist by determining a broad spectrum of LV rotation parameters in different age groups, using speckle tracking echocardiography (STE). The final study population consisted of 61 healthy volunteers (16–35 yr, n = 25; 36–55 yr, n = 23; 56–75 yr, n = 13; 31 men). LV peak systolic rotation during the isovolumic contraction phase (Rotearly), LV peak systolic rotation during ejection (Rotmax), instantaneous LV peak systolic twist (Twistmax), the time to Rotearly, Rotmax, and Twistmax, and rotational deformation delay (defined as the difference of time to basal Rotmax and apical Rotmax) were determined by STE using QLAB Advanced Quantification Software (version 6.0; Philips, Best, The Netherlands). With increasing age, apical Rotmax (P < 0.05), time to apical Rotmax (P < 0.01), and Twistmax (P < 0.01) increased, whereas basal Rotearly (P < 0.001), time to basal Rotearly (P < 0.01), and rotational deformation delay (P < 0.05) decreased. Rotational deformation delay was significantly correlated to Twistmax (R² = 0.20, P < 0.05). In conclusion, Twistmax increased with aging, resulting from both increased apical Rotmax and decreased rotational deformation delay between the apex and the base of the LV. This may explain the preservation of LV ejection fraction in the elderly.

AGING AFFECTS ALL COMPONENTS of the heart (muscular, valvular, and vascular) (12). As the number and proportion of aged individuals in the population increases, quantitative information on age-associated changes in cardiovascular function in the absence of disease becomes more important to define the specific characteristics of the cardiovascular aging process and eventually to target relevant age-associated changes for therapeutic intervention.

Left ventricular (LV) twist describes the instantaneous circumferential motion of the apex with respect to the base of the heart and has an important role in LV function (4, 9). Recently, speckle tracking echocardiography (STE) has been introduced as a new method for angle-independent quantification of LV twist (8, 17). Speckles are natural acoustic markers that occur as small and bright elements in conventional gray-scale ultrasound images. The speckles are the result of constructive and destructive interference of ultrasound, back-scattered from structures smaller than a wavelength of ultrasound (3). This gives each small area a rather unique speckle pattern that remains relatively constant from one frame to the next. Therefore, a suitable pattern-matching algorithm can identify the frame-to-frame displacement of a speckle pattern, allowing myocardial motion to be followed in two dimensions. Age-related changes in LV twist have been reported in previous studies (15, 29).

This study sought to investigate the biomechanics behind age-related changes in LV twist in more detail by determining a broad spectrum of LV rotation parameters and the timing of these parameters in different age groups using STE.

METHODS

Study participants. Subjects were primarily recruited from our department (personnel) or were family members or friends. The study population consisted of 98 healthy, nonobese (body mass index <27 kg/m²) volunteers without hypertension, diabetes, or regular use of medication for cardiovascular disease, with a normal 12-lead electrocardiogram, normal left atrial and LV dimensions, and LV function by transthoracic echocardiography. None of the patients had complaints compatible with cardiac disease. An informed consent was obtained from all subjects and the institutional review board approved the study.

Echocardiography. Echocardiographic studies were performed with a commercially available system (iE33; Philips, Best, The Netherlands), equipped with a broadband S5-1 transducer (frequency transmitted 1.7 MHz, received 3.4 MHz), by a single, experienced sonographer (W. B. Vletter). All echocardiographic measurements were averaged from 3 heartbeats. From the second harmonic M-mode recordings, the following data were acquired: left atrial size, LV end-diastolic septal and posterior wall thickness, and LV end-diastolic and end-systolic dimension. LV ejection fraction was calculated from LV volumes by the modified biplane Simpson rule in accordance with the guidelines (25). 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 were measured. The duration of the isovolumic and ejection phase were determined using pulsed-wave Doppler velocity data of both the LV inflow and outflow tract. Tissue Doppler was applied end-expiratory in the pulsed-wave Doppler mode at the level of the inferoseptal side of the mitral annulus from an apical 4-chamber view. To acquire the highest wall tissue velocities, the angle between the Doppler beam and the longitudinal motion of the investigated structure was minimized. The spectral pulsed-wave Doppler velocity range was adjusted to obtain an appropriate scale. The velocities of the mitral annular systolic wave (Sm), early diastolic wave (Em), and late diastolic wave (Am) were noted.

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To optimize speckle tracking, two-dimensional gray-scale harmonic images were obtained at a frame rate of 60–80 frames/s. Parasternal short-axis images at the LV basal level (showing the tips of the mitral valve leaflets) with the cross section as circular as possible were obtained from the standard parasternal position, defined as the position in which the LV and aorta were most in-line with the mitral valve tips in the middle of the sector. To obtain a short-axis image at the LV apical level (just proximal to the level with end-systolic LV luminal obliteration), the transducer was positioned 1 or 2 intercostal spaces more caudal as previously described by us (31). From each short-axis level, 3 consecutive end-expiratory cardiac cycles were acquired and transferred to a QLAB workstation (Philips) for off-line analysis.

Speckle tracking analysis. Analysis of the datasets was performed using QLAB Advanced Quantification Software version 6.0 (Philips), which was recently validated against magnetic resonance imaging (MRI) for assessment of LV twist (7). To assess LV rotation, six tracking points were placed manually (after gain correction) on an end-diastolic frame on the mid-myocardium in each parasternal short-axis image. Tracking points were separated about 60° from each other and placed on 1 (30°, anteroseptal insertion into the LV of the right ventricle), 3 (90°), 5 (150°), 7 (210°), 9 (270°, inferoseptal insertion into the LV of the right ventricle), and 11 (330°) o’clock to fit the total LV circumference (Fig. 1).

If a tracking point showed poor speckle tracking by visual assessment, the position of the tracking point was manually changed on the end-diastolic frame in a circumferential direction toward one of the other tracking points but not more than 1 h. When speckle tracking was still insufficient, the position of the tracking point could be changed additionally in the direction of the endocardium. Because all tracking points are needed for optimal measurement of global LV rotation, a subject was considered insufficient for analysis of global LV rotation by STE and excluded when, despite these changes, one or more tracking points still did not track well.

Data were exported to a spreadsheet program (Excel; Microsoft, Redmond, WA) to determine LV peak systolic rotation during the isovolumic contraction phase (Rotearly), LV peak systolic rotation during ejection (Rotmax), time to Rotearly (from R wave to Rotearly), and time to Rotmax (from R wave to Rotmax). Instantaneous LV peak systolic twist (Twistmax, defined as the maximal value of instantaneous apical LV systolic rotation − basal LV systolic rotation), instantaneous LV peak systolic torsion (Torsionmax) (Fig. 2), and time to Twistmax were assessed as well. Torsionmax was defined as Twistmax divided by the LV diastolic longitudinal length between the LV apex and the mitral plane. Rotational deformation delay was defined as the difference of time to basal Rotmax and time to apical Rotmax. A positive rotational deformation delay value indicates a shorter time to apical Rotmax than time to basal Rotmax. To adjust for intra- and intersubject differences in heart rate, the time sequence was normalized to the percentage of systolic duration. End-systole was defined as the point of aortic valve closure. In each study, it was verified that heart rate for the cardiac cycle in which the timing of aortic valve closure was assessed was the same as the cardiac cycle used for analysis of LV rotation parameters.

Statistical analysis. Measurements are presented as means ± SD. Continuous variables were compared using Student’s t-test or ANOVA when appropriate. Simple linear regression of LV rotation parameters against age was performed. Relationships between different parameters were assessed by correlation analysis. A P value < 0.05 was considered statistically significant. Intraobserver and interobserver variability for Twistmax in our center are 6 ± 6 and 9 ± 5%, respectively (30).

RESULTS

Feasibility of obtaining LV rotation parameters. In 28 subjects (29%), image quality of the LV basal level was insufficient for STE analysis. The LV apical level was excluded from analysis in 34 subjects (35%) because of either the inability to obtain a short-axis image at the LV apical level from an intercostal space more caudal than the standard position (7%) or because of insufficient image quality (27%). In the remaining 61 subjects (62%) that made up the final study group, both the LV basal and apical levels were available, facilitating complete analysis of all LV rotation parameters. These subjects were classified into 3 groups, aged 16–35 (group 1, n = 25), 36–55 (group 2, n = 23), and 56–75 (group 3, n = 13) yr. The proportion of

Fig. 1. Left: positioning of the tracking points at the left ventricular (LV) basal (top) and apical level (bottom). Right: LV rotation time curves. The green line represents LV rotation, the blue line the area within the circle of tracking points, and the white line recruitment, which was not activated in this example. The electrocardiogram is displayed at the bottom (thin, green line).
subjects that was excluded was comparable between the different age groups (group 1, 36%; group 2, 39%; group 3, 40%; P = not significant). The need to adjust the intended position of a tracking point in a circumferential direction (7 vs. 7 vs. 8% of the tracking points in group 1 vs. 2 vs. 3, respectively) or toward the endocardium (2 vs. 3 vs. 2% of the tracking points in group 1 vs. 2 vs. 3, respectively) was comparable between the different age groups as well.

**General characteristics of the final study population.** The clinical and echocardiographic characteristics of the different age groups are shown in Table 1. Apart from left atrial size (P < 0.001), there were no significant differences in clinical characteristics or cardiac dimensions between the groups. Doppler measurements revealed that the E/A and Em/Am ratio decreased with advancing age (both P < 0.001).

**Relation of LV rotation parameters to aging.** Several differences in LV rotation parameters were identified between the different age groups (Table 2 and Fig. 3). With increasing age, apical Rotmax (P < 0.05), time to apical Rotmax (P < 0.01), Twistmax (P < 0.01), and Torsionmax (P < 0.01) increased, whereas basal Rotearly (P < 0.001), time to basal Rotearly (P < 0.01), and rotational deformation delay (P < 0.05) decreased. Nevertheless, rotational deformation delay remained positive in all age groups, indicating a shorter time to apical Rotmax than to basal Rotmax (Fig. 4).

Linear regression analysis showed comparable changes of LV rotation parameters with advancing age (Fig. 5). Age was significantly correlated to basal Rotearly, apical Rotmax, Twistmax, Torsionmax, time to basal Rotearly, time to apical Rotmax, and rotational deformation delay. Although there was no significant difference in time to Twistmax during aging shown by linear regression.

**Mutual relation between LV rotation parameters.** After adjustment for age, no significant correlation could be identified between basal Rotearly, basal Rotmax, apical Rotearly, apical Rotmax, and the timing of these parameters. Nevertheless, rotational deformation delay retained significantly correlated to Twistmax (R² = 0.20, P < 0.05) and Torsionmax (R² = 0.23, P < 0.05).

**DISCUSSION**

The main findings of this study are increased instantaneous LV twist and torsion with aging, resulting from both increased counterclockwise apical Rotmax and decreased...
rotational deformation delay between the apex and the base of the LV.

LV rotation parameters during isovolumic contraction. LV rotation and twist originate from the dynamic interaction between oppositely wound epicardial and endocardial myocardial fiber helices (2). During isovolumic contraction, the LV base shows, as viewed from the apex, a counterclockwise rotation, whereas the LV apex shows a less pronounced clockwise rotation. This phenomenon has been described previously in experimental studies (10, 27) and is explained by the predominant mechanical activity that develops along the right-handed subendocardial helix of myocardial fibers during isovolumic contraction. The shortening of this right-handed helix is accompanied by stretching of the outer subepicardial fibers (left-handed helix) (6, 26). This bipolaric deformation satisfies isovolumic mechanics: shortening in one direction is accompanied with stretching in the other direction (Fig. 6). Furthermore, stretching of myofibers during isovolumic contraction is important in initiating a "stretch activation response," an intrinsic length-sensing mechanism that allows muscle to adjust the force and duration of subsequent shortening (5).

MRI studies, the counterclockwise basal Rot early was recognized, but the clockwise apical Rot early was not observed (13). The low temporal resolution of tagged MRI might be the reason why the less pronounced and earlier occurring clockwise apical Rot early was not recognized. Our study is the first to investigate the temporal dispersion of basal and apical Rot early. Time to basal Rot early takes more than twice as long as time to apical Rot early (32 ± 9 vs. 13 ± 6 ms). This may be explained by the start of electrical activation subendocardially in the right-handed helix near the apical septum with subsequent spread of the electrical activity toward the base (24).

LV rotation parameters during ejection. Consistent with previous studies (8, 17, 21), basal Rot max was clockwise, whereas apical Rot max was counterclockwise. During ejection, the left-handed epicardial helix of myocardial fibers pulls the base clockwise and the apex counterclockwise. The right-handed helix in the endocardium tries to do the opposite, but because the epicardium is farther from the centerline, the epicardial helix torque is greater and thus dominates the rotation (28).

Rotational deformation delay had a positive value, indicating a shorter time to apical Rot max than to basal Rot max. An explanation for this finding is provided in recent investigations. Ramanathan et al. (23) showed that the earliest...
electrical epicardial breakthrough occurs in the right ventricular free wall and the anterior LV wall and then travels in an apex-to-base direction. The basal posterior wall was the last region to be activated. Sengupta et al. (27) showed that the apex-to-base delay in mechanical shortening of the LV parallels the apex-to-base direction of the electric activation sequence. To our knowledge, our study is the first to recognize the apex-to-base temporal dispersion in LV rotation.

Influence of advancing age on LV rotation parameters. The increasing number and proportion of aged individuals in the population warrants knowledge of normal physiological changes of LV biomechanics with advancing age. Counterclockwise basal Rotearly decreased and counterclockwise
apical Rotmax increased with advancing age. Interestingly, basal Rotearly is caused by, whereas apical Rotmax is inhibited by, the right-handed subendocardial helix of myocardial fibers. The function of subendocardial fibers declines with age, even in normal hearts (14, 16), providing a rational explanation for these findings. On the other hand, it remains unsolved why apical Rotearly and basal Rotmax thought to be influenced in the same manner by the right-handed subendocardial helix of myocardial fibers, are less affected by age. In accordance with our study, in a study by Notomi et al. (18), basal Rotmax was also less influenced by age.

Global LV systolic function is known to be preserved in older individuals (20, 33). Our findings of increased Twistmax and Torsionmax with advancing age are in agreement with previous studies (15, 19, 29) and elucidate a possible contribution of Twistmax and Torsionmax to preserve ejection fraction in the elderly. Of note, it is the helical fiber architecture of the heart that doubles the LV ejection fraction (22). Thus optimization of LV twist is an effective method to preserve LV systolic function. Increased Twistmax and Torsionmax with advancing age has been explained by an increase in apical Rotmax, but the decrease in rotational deformation delay with advancing age may also play an important role. Time to basal Rotmax remains relatively unchanged with aging, whereas apical Rotmax occurs later in systole with advancing age, approaching the time to basal Rotmax and thereby decreasing rotational deformation delay. The decrease in rotational deformation delay will increase Twistmax and Torsionmax because both are determined by instantaneous basal and apical Rotmax. The finding of a significant, after adjustment for age, negative correlation between rotational deformation delay and Twistmax and Torsionmax further supports this. Although the increase in time to apical Rotmax might be caused by an increase in elastic and collagenous tissue in the conduction system with advancing age (12), this would implicate an increase in time to basal Rotmax as well, leaving rotational deformation delay unchanged. The increase in time to apical Rotmax with advancing age may also be explained by prolonged contraction duration, which was previously found in aged myocardium of animals (11, 32). This prolonged contraction duration results from a prolonged active state rather than changes in passive properties or myocardial catecholamine content (11). Whether this is the true explanation of the increase in time to apical Rotmax with advancing age, and why time to basal Rotmax would not be influenced by this phenomenon, needs to be clarified in further studies. Nevertheless, both increased apical Rotmax and decreased rotational deformation delay seem to be characteristics of “physiological cardiac aging” and may contribute to the preservation of LV systolic function in the elderly.

Limitations. The echocardiographic window is the Achilles’ heel of echocardiography. Therefore, a relatively large amount of the subjects had to be excluded from analysis because image quality in one or more segments was insufficient for STE analysis. In our experience, for reliable speckle tracking using QLAB Advanced Quantification Software, at least moderate image quality is mandatory. The current paper provides further insight into the process of cardiac aging. However, whether changes in the extent and timing of LV rotation with age are of clinical importance remains unsolved. Therefore, clinical studies are needed to test the utility and importance of the assessment of LV rotation parameters by STE in daily clinical practice. In a small subset of subjects, it was necessary to adjust the intended position of a tracking point in a direction toward the endocardium. It is possible that the extent of the measured LV rotation in these subjects was slightly overestimated because it is known that LV rotation increases from the epicardium to the endocardium (1). However, the number of tracking points in which changing the position toward the endocardium was needed was small and equally distributed among the different age groups. Consequently, we believe that a significant influence on the results is unlikely.
REFERENCES


