Left ventricular strain and strain rate in a general population

Tatiana Kuznetsova¹, Lieven Herbots², Tom Richart¹, Jan D’hooge³, Lutgarde Thijs¹, Robert H. Fagard¹, Marie-Christine Herregods², and Jan A. Staessen*¹

¹The Studies Coordinating Centre, Division of Hypertension and Cardiovascular Rehabilitation, University of Leuven, Campus Gasthuisberg, Herestraat 49, Box 702, B-3000 Leuven, Belgium; ²Division of Cardiology, Department of Cardiovascular Disease, University of Leuven, Leuven, Belgium; and ³Division of Cardiovascular Imaging and Dynamics, Department of Cardiovascular Disease, University of Leuven, Leuven, Belgium

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Aims

Strain and strain rate (SR) are measures of deformation that reflect left ventricular (LV) function. To our knowledge, no previous study described these indexes in a general population. We therefore described peak-systolic strain and SR of the LV in the general population and derived diagnostic thresholds for these measurements in a healthy subgroup.

Methods and results

In 480 subjects enrolled in a family-based population study (50.5% women; mean age, 50.5 years; 37.2% hypertensive), we measured: (i) end-systolic longitudinal strain and peak-systolic SR from the basal portion of the LV inferior and inferolateral free walls; (ii) radial deformation of the LV inferolateral wall. Longitudinal (mean, 22.9%) and radial (59.2%) strain and longitudinal (1.31 s⁻¹) and radial (3.40 s⁻¹) SR decreased with age (P < 0.007). Longitudinal and radial strain independently decreased (P < 0.006) with relative wall thickness (RWT), longitudinal strain with the waist-to-hip ratio, and radial strain with body weight. In contrast, LV ejection fraction increased (P < 0.0001) with age and RWT. Longitudinal and radial strain rate increased with heart rate (P < 0.05). In healthy subgroup (n = 236), the fifth percentiles were 18.4 and 44.3%, and 0.99 and 2.43 s⁻¹, for longitudinal and radial strain and SR, respectively.

Conclusion

We explored the early signs of LV systolic dysfunction in a general population, using tissue Doppler imaging technique. LV strain and SR decrease with age, body weight, central obesity, and RWT. Our current study resulted in the proposal for diagnostic thresholds for strain and SR, based on a healthy subgroup recruited via random sampling of the population.

Keywords

Echocardiography • Population • Left ventricular function • Strain

Introduction

Symptomatic heart failure is a serious disease with high mortality.¹ In general, progression of myocardial dysfunction to heart failure reflects remodelling of the left ventricle (LV). Because the process of remodelling begins before the onset of symptoms, the recent guidelines place special emphasis on detecting subclinical LV systolic and diastolic dysfunction.¹ The echocardiographic techniques to assess early changes in systolic and diastolic LV function evolved rapidly over the past years.² New techniques of tissue Doppler imaging (TDI) and tissue tracking provide additional information about cardiac function over and beyond classical M-mode and two-dimensional (2D) echocardiography and pulse wave Doppler. On the basis of colour Doppler myocardial imaging, 1D regional strain and strain rate (SR) curves can be calculated by comparing local myocardial velocity profiles.³ Echocardiographic velocity-based SR imaging has been applied for the assessment of resting ventricular function and myocardial viability during stress testing for ischaemia.⁴ To our knowledge, no study described the distributions and determinants of the peak-systolic...
strain and SR in the general population. In the absence of an outcome-driven reference frame, we used the distribution of the aforementioned indexes in normotensive subjects without cardiovascular disease to determine preliminary thresholds distinguishing normal from abnormally low values in the general population.

**Methods**

**Study participants**

The Ethics Committee of the University of Leuven approved the Flemish Study on Environment, Genes and Health Outcomes (FLE-MENGO). From August 1985 until December 2005, we identified a random population sample stratified by sex and age from a geographically defined area in northern Belgium. The seven municipalities gave listings of all inhabitants sorted by address. Households, defined as those who lived at the same address, were the sampling unit. We numbered households consecutively, and generated a random number list by use of SAS random function. Households with a number matching the list were invited; household members >18 years were eligible. We re-invited 690 former participants for a follow-up examination including echocardiography, at our field centre. After excluding 20 patients who were bed-ridden or institutionalized, we obtained informed written consent from 553 subjects (participation rate, 82%). We excluded a further 48 subjects with overt cardiac diseases, because of myocardial infarction or coronary revascularization. Excluded a further 48 subjects with overt cardiac diseases, because of moderate or severe valvular abnormalities (version 4.6.2), allows M-mode tracking of the myocardium to ensure that the sample volume is maintained in the same anatomical position within myocardial image throughout the cardiac cycle. We positioned the sampling volume in the basal portion of the interroged wall at the level of the posterior chordae tendineae. To compute end-systolic strain and peak-systolic SR, from now on referred to as strain and SR, we averaged three consecutive cycles. We calculated the radial SR of the infero-lateral wall and the longitudinal SR of the inferior and infero-lateral walls by measuring the spatial velocity gradient over a computational area of 5 and 10 mm, respectively. Natural strain profiles were obtained by integrating the mean SR profile over time (see Supplementary material online, Figure S1). The beginning and ending of the ejection phase were determined from the simultaneously recorded ECG and the continuous-wave Doppler velocity trace at the level of the aortic valve. We used lateral averaging of 3–5 beams/pixels. Because there were no differences between the infero-lateral and infero-lateral walls in longitudinal strain and SR, for statistical analysis, we averaged these measurements and used their absolute values.

Two sonographers analysed recorded images, averaging three heart cycles for statistical analysis, using a workstation running the EchoPac, version 4.0.4 (GE Vingmed, Horten, Norway) software package. The LV internal diameter and interventricular septal and posterior wall thickness were measured at end-diastole from the 2D guided M-mode tracing, as described in the American Society of Echocardiography guideline. End-diastolic LV dimensions were used to calculate LV mass by an anatomically validated formula. Relative wall thickness (RWT) was calculated as the ratio of (interventricular septum + posterior wall thickness)/LV internal diameter at end-diastole. LV end-systolic and end-diastolic volumes and ejection fraction (EF) were calculated with the use of Teicheltz’s method.

We extracted strain and SR curves off-line from colour tissue Doppler images, using dedicated software. The SPEQLE package (version 4.6.2), allows M-mode tracking of the myocardium to ensure that the sample volume is maintained in the same anatomical position within myocardial image throughout the cardiac cycle. We positioned the sampling volume in the basal portion of the interroged wall at the level of the posterior chordae tendineae. To compute end-systolic strain and peak-systolic SR, from now on referred to as strain and SR, we averaged three consecutive cycles. We calculated the radial SR of the infero-lateral wall and the longitudinal SR of the inferior and infero-lateral walls by measuring the spatial velocity gradient over a computational area of 5 and 10 mm, respectively. Natural strain profiles were obtained by integrating the mean SR profile over time (see Supplementary material online, Figure S1). The beginning and ending of the ejection phase were determined from the simultaneously recorded ECG and the continuous-wave Doppler velocity trace at the level of the aortic valve. We used lateral averaging of 3–5 beams/pixels. Because there were no differences between the infero-lateral and infero-lateral walls in longitudinal strain and SR, for statistical analysis, we averaged these measurements and used their absolute values.

Data acquisition

One experienced physician (T.K.) did the ultrasound examination according to the recommendations of the American Society of Echocardiography, using a Vivid7 Pro (GE Vingmed, Horten, Norway) interfaced with a 2.5 MHz phased-array probe. With the subjects in partial left decubitus and breathing normally, the observer obtained images, together with a simultaneous ECG signal, from the parasternal long and short axes and from the apical four-chamber, two-chamber and long-axis views. All recordings included at least five cardiac cycles and were digitally stored for off-line analysis. M-mode echocardiograms of the LV were recorded from the parasternal long-axis view under control of the 2D image. The ultrasound beam was positioned just below the mitral valve at the level of the posterior chordae tendineae.

Using TDI, the observer recorded low-velocity, high-intensity myocardial signals at a high frame rate (>190 fps), while adjusting the imaging angle to ensure a parallel alignment of the ultrasound beam with the myocardial segment of interest. The Nyquist limit was set as low as possible avoiding aliasing.

**Echocardiography**

The participants refrained from smoking, heavy exercise, and drinking alcohol or caffeine-containing beverages for at least 3 h before echocardiography. The blood pressure during echocardiography was the average of two readings, obtained at the end of the examination with a validated OMRON 705IT device (Omron Corp., Tokyo, Japan).

**Other measurements**

At the examination centre, trained study nurses administered a questionnaire to collect detailed information on each subject’s medical history, smoking and drinking habits, and intake of medications. Hypertension was defined as a blood pressure of at least 140 mmHg systolic or 90 mmHg diastolic (average of five consecutive auscultatory readings at the examination centre) or as the use of antihypertensive drugs. Body mass index was weight in kilograms divided by the square of height in meters. Obesity was defined as a body mass index ≥30 kg/m². Waist and hip circumferences were measured to the nearest centimetre with a tape measure while the subject was standing. Abdominal obesity was a waist circumference >102 cm in men and >88 cm in women. Diabetes was a fasting blood glucose of >6.7 mmol/L or use of insulin or oral antidiabetic agents. LV hypertrophy was defined as LV mass index of >125 g/m² for men and >110 g/m² for women. To generate a healthy reference sample, we excluded participants if at least one of the following criteria was fulfilled:
We compared means and proportions by means of a large sample moment about the mean divided by the cube of the standard deviation. Departure from normality was evaluated by Shapiro–Wilk’s statistics and skewness by computation of the coefficient of skewness, i.e. the third moment about the mean divided by the cube of the standard deviation. We computed the variance inflation factor (VIF), and the adjusted R². In the multivariate regression models for longitudinal and radial SR, we did not detect collinearity (VIF < 1.00). Although VIF was close to 1 (VIF < 1.40) in the regression models for longitudinal and radial strain, we applied ridge regression. It allows better interpretation of the regression coefficients by imposing some bias (ridge regression)

| Characteristics                  | Women (n = 243) | Men (n = 237) | P-value |
|----------------------------------|-----------------|---------------|---------|
| Clinical measurements            |                 |               |         |
| Anthropometrics                  |                 |               |         |
| Age (years)                      | 51.5 ± 14.0     | 50.4 ± 15.5   | 0.36    |
| Height (cm)                      | 162.8 ± 6.6     | 175.0 ± 7.1   | <0.0001 |
| Weight (kg)                      | 69.4 ± 13.1     | 80.5 ± 10.9   | <0.0001 |
| Body mass index (kg/m²)          | 26.2 ± 4.5      | 26.3 ± 3.3    | 0.80    |
| Waist circumference (cm)         | 84.2 ± 11.3     | 92.4 ± 9.7    | <0.0001 |
| Waist-to-hip ratio               | 0.82 ± 0.06     | 0.91 ± 0.07   | <0.0001 |
| Systolic pressure (mmHg)         | 129.9 ± 19.8    | 133.5 ± 14.9  | 0.02    |
| Diastolic pressure (mmHg)        | 76.3 ± 9.0      | 77.6 ± 8.9    | <0.0001 |
| Heart rate (beats/min)           | 62.7 ± 9.0      | 58.3 ± 8.7    | <0.0001 |
| Questionnaire data               |                 |               |         |
| Current smoking, n (%)           | 51 (21.0)       | 57 (24.0)     | 0.44    |
| Drinking alcohol, n (%)          | 67 (27.6)       | 140 (59.1)    | <0.0001 |
| Hypertensive, n (%)              | 89 (36.6)       | 93 (39.2)     | 0.61    |
| Treated for hypertension, n (%)  | 56 (23.0)       | 44 (18.6)     | 0.17    |
| Echocardiographic measurements   |                 |               |         |
| Conventional echocardiography    |                 |               |         |
| LV internal diameter (cm)        | 4.80 ± 0.39     | 5.26 ± 0.44   | <0.0001 |
| Interventricular septum (cm)     | 0.93 ± 0.15     | 1.04 ± 0.17   | <0.0001 |
| Posterior wall (cm)              | 0.82 ± 0.14     | 0.91 ± 0.14   | <0.0001 |
| Relative wall thickness          | 0.37 ± 0.071    | 0.37 ± 0.072  | 0.44    |
| LV mass index (g/m²)             | 82.6 ± 16.5     | 98.0 ± 19.8   | <0.0001 |
| Ejection fraction (%)            | 69.6 ± 7.4      | 67.8 ± 7.2    | 0.009   |
| Stroke volume (mL)               | 75.3 ± 15.2     | 91.8 ± 18.4   | <0.0001 |
| TDI                              |                 |               |         |
| Averaged longitudinal            |                 |               |         |
| Strain (%)                       | 23.0 ± 3.68     | 22.7 ± 3.57   | 0.38    |
| Strain rate (s⁻¹)                | 1.31 ± 0.26     | 1.31 ± 0.23   | 0.66    |
| Radial                          |                 |               |         |
| Strain (%)                       | 60.7 ± 12.5     | 57.6 ± 12.8   | 0.02    |
| Strain rate (s⁻¹)                | 3.44 ± 0.86     | 3.34 ± 0.82   | 0.32    |

Values are mean (±SD) or number of subjects (%); LV, left ventricle.

Numbers of women and men are 199 and 201, respectively.

hypertension (n = 182), diabetes (n = 7), obese (n = 79) or abdominal obesity (n = 108), or LV hypertrophy (n = 43). The number of subjects in the healthy reference group totalled 236 for longitudinal strain and SR, and 214 for the radial measurements.

**Statistical methods**

For database management and statistical analysis, we used SAS software, version 9.1 (SAS Institute, Cary, NC, USA). The central tendency and the spread of the data are reported as mean ± SD. We performed single and stepwise multiple regression to assess the independent correlations of strain and SR with sex, age, height, weight, body mass index, waist circumference, waist-to-hip ratio (WHR), heart rate, systolic and diastolic blood pressures during the echocardiographic examination, RVWT, LV posterior wall thickness, and end diastolic LV diameter. We set the P-values for variables to enter and stay in the regression models at 0.10. We ran regression diagnostics to exclude that possible collinearity inappropriately influenced our multivariate models. In linear regression we computed the variance inflation factor (VIF), and the adjusted R². In the multivariate regression models for longitudinal and radial SR, we did not detect collinearity (VIF < 1.00). Although VIF was close to 1 (VIF < 1.40) in the regression models for longitudinal and radial strain, we applied ridge regression. It allows better interpretation of the regression coefficients by imposing some bias (ridge regression
Figure 1 Distribution of the longitudinal (A, C) and radial (B, D) strain and strain rate in individuals drawn at random from the general population.

Figure 2 Longitudinal (square) and radial (triangle) strain and strain rate by age. Values are mean ± SEM.
control value – k) on the regression coefficients and shrinking their variances. Finally, we checked the stability of our regression models, by determining the bootstrap distribution of the partial regression coefficients by randomly resampling the study population 1000 times with replacement, using the PROC SURVEYSELECT procedure, as implemented in the SAS package.6 We calculated the bootstrap point estimates and 95% confidence intervals as the mean ± 1.96 SE of the bootstrap distribution. We also computed the confidence interval of the fifth percentile in the reference group, using the similar bootstrap procedure.6

Results
Characteristics of participants
The 480 participants included 243 (50.6%) women, and 182 (37.2%) hypertensive patients of whom 100 (20.8%) were on anti-hypertensive drug treatment. Table 1 shows the clinical and echocardiographic characteristics of the study participants by sex. Women compared with men had lower systolic and diastolic blood pressures, higher heart rate, and less frequently reported intake of alcohol (Table 1). The echocardiographic measurements reflecting LV size (Table 1) and systolic function were greater in men than in women.

Distribution of systolic strain and strain rate
In all subjects, the distribution of the longitudinal strain was close to normal (P = 0.94, Figure 1A); the coefficient of skewness was 0.022. The distribution of the radial strain departed from normality and was positively skewed (P = 0.016; Figure 1B) with the coefficient of skewness amounting to 0.29. Similarly, the longitudinal and radial SRs were positively skewed (P < 0.001, Figure 1C and D). The coefficients of skewness were 0.88 and 1.03, respectively.

Strain averaged 22.9% (95% confidence interval 17.0–28.9%; n = 480) longitudinal and 59.2% (40.1–82.0%; n = 400) radial. SR averaged 1.31 s⁻¹ (0.94–1.73 s⁻¹; n = 480) longitudinal and 3.40 s⁻¹ (2.17–4.74 s⁻¹; n = 400) radial. Table 1 lists the mean values of the longitudinal and radial strain by gender. Women and men had similar longitudinal strain and SR. However, the radial strain (P = 0.025), but not SR (P = 0.32) was significantly higher in women than in men.

Determinants of strain and strain rate in a general population
In univariate regression analyses, longitudinal and radial strain and SR significantly (P < 0.0001) decreased with age (Figure 2) and RWT (Figure 3A and B). These associations with age and RWT
Table 2  Correlates of the longitudinal and the radial strain and strain rates and ejection fraction selected by stepwise regression

| Parameter            | Averaged longitudinal Strain (%) | Strain rate (s⁻¹) | Radial Strain (%) | Strain rate (s⁻¹) | Ejection fraction (%) |
|----------------------|----------------------------------|------------------|------------------|------------------|----------------------|
| Adjusted R²          | 0.010                            | 0.072            | 0.077            | 0.050            | 0.129                |
| Ridge control value  | 0.1                              | 0                | 0.075            | 0                | 0.075                |
| **Regression statistics** |                                  |                  |                  |                  |                      |
| Age (+10 years)      | $-0.29 \pm 0.11$                 | $-0.040 \pm 0.0073$ | $-1.19 \pm 0.43$ | $-0.11 \pm 0.029$ | $1.11 \pm 0.22$ |
|                      | (−0.50 to −0.072); $P = 0.007$; VIF = 1.02 | (−0.053 to −0.025); $P < 0.0001$; VIF = 1.00 | (−2.03 to −0.35); $P = 0.005$; VIF = 1.01 | (−0.17 to −0.059); $P < 0.0001$; VIF = 1.00 | (0.67 to 1.52); $P < 0.0001$; VIF = 1.02 |
| Sex (women)          | —                                | —                | —                | —                | $1.70 \pm 0.59$ (0.54 to 2.85); $P = 0.004$; VIF = 0.87 |
| Body weight (+1 kg)  | —                                | —                | $-0.14 \pm 0.044$ | —                |                      |
|                      | $P = 0.0001$; VIF = 0.93         |                  | (−0.22 to −0.05); $P = 0.002$; VIF = 0.88 |                  |                      |
| Waist-to-hip ratio (+0.1) | $-0.63 \pm 0.91$              | —                | —                | —                |                      |
|                      | (−1.04 to −0.25); $P = 0.0001$; VIF = 0.93 |                  |                  |                  |                      |
| Heart rate (+10 beats/min) | —                                | $0.034 \pm 0.012$ | —                | $0.08 \pm 0.044$ | —                    |
|                      | 0.012 to 0.058; $P = 0.002$; VIF = 1.00 |                  | (0.0001 to 0.17); $P = 0.05$; VIF = 1.00 |                  |                      |
| RWT (+0.1)           | $-0.77 \pm 0.22$                 | —                | $-2.48 \pm 0.91$ | —                | $1.74 \pm 0.45$ |
|                      | (−1.20 to −0.34); $P = 0.0005$; VIF = 0.97 |                  | (−4.26 to −0.70); $P = 0.006$; VIF = 1.02 |                  | (0.85 to 2.63); $P = 0.0001$; VIF = 1.01 |

Values are mutually adjusted partial regression coefficient ± SE (95% confidence interval). RWT, relative wall thickness. VIF, variance inflation factor.
were mutually independent (Table 2). Longitudinal strain also decreased with WHR \( (P = 0.001; \text{Figure } 3C) \) and radial strain with body weight \( (P = 0.002; \text{Figure } 3D) \). While adjusting for age, longitudinal \( (P = 0.002) \) and radial \( (P = 0.05) \) SR increased with heart rate. In contrast, EF increased with age \( (P < 0.0001) \) and RWT \( (P = 0.0001) \). The explained variance totalled 10 and 7.7\% for the longitudinal and radial strain, and 7.2 and 5.0\% for the longitudinal and radial SR, respectively. Table 3 shows the bootstrap distribution of the partial regression coefficients based on 1000 repetitions.

### Strain and strain rate in the healthy subgroup

In the selected healthy subjects, strain averaged 23.6\% (18.4–29.4\%; \( n = 236 \)) longitudinal and 61.4\% (44.3–84.4\%; \( n = 214 \)) radial. SR averaged 1.34 \( \text{s}^{-1} \) (0.99–1.91 \( \text{s}^{-1} \); \( n = 236 \)) longitudinal and 3.49 \( \text{s}^{-1} \) (2.43–4.68 \( \text{s}^{-1} \); \( n = 214 \)) radial. Table 4 provides detailed statistics for the longitudinal and radial strain and SR by age in the reference group.

In the last step of our analyses, we rounded upwards the fifth percentiles in the reference group to the next integer value ending in zero or five. This procedure suggested as lower thresholds for normal myocardial deformation patterns, absolute percentiles in the reference group to the next integer value and 3.49 \( \text{s}^{-1} \) radial. SR averaged 1.34 \( \text{s}^{-1} \) (0.99–1.91 \( \text{s}^{-1} \); \( n = 236 \)) longitudinal and 3.49 \( \text{s}^{-1} \) (2.43–4.68 \( \text{s}^{-1} \); \( n = 214 \)) radial. Table 4 shows the bootstrap distribution of the partial regression coefficients based on 1000 repetitions.

### Discussion

We determined the distributional characteristics of LV strain and SR in a random population sample. The strain in all participants aged 17–89 years averaged 22.9\% longitudinal and 59.2\% radial. SR averaged 1.31 \( \text{s}^{-1} \) longitudinal and 3.40 \( \text{s}^{-1} \) radial. Our current findings, to our knowledge the first based on a general population, are in line with previous reports in selected healthy subjects.\(^8\) Mean values ranged from 15 to 25\% for longitudinal strain, from 50 to 70\% for radial strain, from 1.0 to 1.4 \( \text{s}^{-1} \) for the longitudinal SR, and from 3.1 to 4.1 \( \text{s}^{-1} \) for the radial SR. The age ranges, over which these mean values were computed, encompassed 20–42 years minimally\(^8\) and 18–79 years maximally.\(^11\) The number of healthy volunteers ranged from 40 to 146.

In our population, longitudinal and radial strain and SR significantly and independently decreased with age and RWT. In contrast, EF increased with age and RWT. Previous studies with radionuclide methods\(^15\) or echocardiography\(^13\) showed that in healthy subjects LV EF at rest does not change, or increase slightly with age. Studies on the effects of age on LV longitudinal strain and SR are scarce. Previous studies in healthy volunteers reported significant effect of aging on systolic longitudinal myocardial velocities but not on longitudinal strain and SR.\(^10\)\(^11\) Andersen and Poulsen\(^14\) recently found that the global longitudinal contraction, as assessed by tissue tracking in 55 healthy subjects, declined with age. In keeping with our observations, studies with TDI\(^15\) or magnetic

### Table 3 Bootstrap distribution of the partial regression coefficients

| Parameter            | Ejection fraction (%) | Strain (%) | Strain rate (\( \text{s}^{-1} \)) | Age (+10 years) | Sex (women) | Body weight (+1 kg) | Waist-to-hip ratio (+0.1) | Heart rate (+10 beats/min) | RWT (+0.1) |
|----------------------|-----------------------|------------|---------------------------------|-----------------|-------------|---------------------|--------------------------|--------------------------|------------|
|                      | 1.03 (0.55 to 1.53)   | -0.099     | 0.009                           | -0.099          | -0.051      | -0.16               | -0.27                    | -0.094                   | -0.023     |
|                      | 2.25 (0.09 to 3.85)   | 0.016      | 0.008                           | 0.008           | 0.029       | 0.28                | 0.19                     | 0.013                    | 0.054      |
|                      | 1.76 (0.87 to 2.67)   | -2.71      | -2.71                           | -2.71           | -2.71       | -2.71               | -2.71                    | -2.71                    | -2.71      |

Values are mutually adjusted partial regression coefficients (95\% confidence interval) as estimated by a bootstrap procedure with 1000 repetitions.
resonance imaging\textsuperscript{16} revealed that longitudinal shortening and/or radial myocardial thickening was lower in patients with LV hypertrophy and normal EF than in normal controls. Patients with LV hypertrophy have increased myocardial fibrosis, particularly in the subendocardium.\textsuperscript{17} The contraction of the myocardial layer, which is located in the subendocardium, is mainly responsible for longitudinal shortening.\textsuperscript{18} Thus, the decreased longitudinal deformation in subjects with LV concentric remodelling may be related to subendocardial fibrosis.

In our study, longitudinal strain decreased with the WHR and radial strain with body weight. Along similar lines, Wong et al.\textsuperscript{19} found that 109 overweight or obese subjects without overt heart disease had a significantly lower averaged long-axis strain compared with 33 referent subjects, whereas there was no difference between groups in LVEF. The obese patients not only had greater chamber size, but also higher tissue density as evidenced by calibrated myocardial backscatter. The latter observation might reflect myocardial fibrosis.\textsuperscript{19} Moreover, a previous study demonstrated that insulin resistance and alterations in myocardial substrate metabolism lead to myocardial contractile dysfunction in young obese women.\textsuperscript{20} Insulin might also influence cardiac geometry via its growth-stimulating, sodium-retaining and other neuroendocrine effects. We could not also exclude that the inverse association between LV strain and central obesity might be the increased intra-abdominal hydrostatic pressure in obese people acting upon the diaphragm and affecting the intrathoracic pressure to such an extent that the transmural filling pressure of the heart is reduced.\textsuperscript{21}

In the healthy participants, enrolled in this study, the fifth percentiles were considered as the lower limits of normality for the longitudinal and radial strain and SR. These values were 18.4%, 44.3%, 0.99 s\textsuperscript{-1} and 2.43 s\textsuperscript{-1}, respectively. In the absence of an outcome-driven reference frame, averaging fifth percentiles in subjects free from cardiovascular diseases and rounding the resulting boundaries upwards to the nearest values ending in zero or five, produced working definitions of normal myocardial deformation patterns, which can be easily remembered. Following this approach, absolute values for normal myocardial deformation in the Flemish population, would be >18.5 and 44.5% for the longitudinal and radial strain, and >1.00 and 2.45 s\textsuperscript{-1} for longitudinal and radial SR. These preliminary threshold values for the population do not account for age. However, in absolute terms, the effect of age on LV deformation is small compared with those of central obesity and LV remodelling.

The present study must be interpreted within the context of its potential limitations and strengths. First, TDI SR imaging is prone to measurement error due to signal noise, acoustic artefacts, and angle dependency.\textsuperscript{4} This may limit the application of TDI in routine clinical practice. Newer techniques, such as ‘speckle tracking’ algorithms, might be less variable. In contrast to TDI parameters, speckle tracking is an angle independent technique as the movement of speckles in 2D grey-scale images can be followed in any direction.

### Table 4 Strain and strain rate in the healthy reference group

| Age          | Longitudinal Strain (%) | Radial Strain (s\textsuperscript{-1}) |
|--------------|-------------------------|---------------------------------------|
|              | <40  | 40–59 | ≥60 | All | <40  | 40–59 | ≥60 | All |
| N            | 79   | 128   | 29  | 236 | 71    | 119   | 24  | 214 |
| X            | 24.2 | 23.5  | 22.3| 23.6| 62.0  | 61.5  | 59.9| 61.4|
| SD           | 3.40 | 3.19  | 3.62| 3.36| 11.6  | 12.2  | 11.8| 11.9|
| P\textsubscript{5} | 18.8 | 18.4  | 16.4| 18.4| 44.3  | 43.9  | 45.6| 44.5|
| P\textsubscript{10} | 20.2 | 19.1  | 16.6| 19.4| 48.5  | 46.2  | 46.0| 46.2|
| P\textsubscript{25} | 21.7 | 21.5  | 20.4| 21.5| 52.7  | 52.0  | 51.9| 52.1|
| P\textsubscript{50} | 23.7 | 23.7  | 23.1| 23.6| 59.9  | 60.6  | 56.4| 60.1|
| P\textsubscript{75} | 27.4 | 25.6  | 24.5| 25.7| 71.1  | 71.0  | 67.8| 70.4|
| P\textsubscript{90} | 29.0 | 27.2  | 27.6| 28.4| 75.6  | 78.7  | 76.7| 78.0|
| P\textsubscript{95} | 29.6 | 29.0  | 27.7| 29.5| 84.5  | 83.4  | 78.4| 84.4|

\textsuperscript{N, X, SD, P\textsubscript{5}, P\textsubscript{10}, P\textsubscript{25}, P\textsubscript{50}, P\textsubscript{90}, P\textsubscript{95} indicate number of subjects, mean, standard deviation and percentiles.}
The 2D technique provides comparable results as TDI for longitudinal strain, but offers a more user-friendly approach. In the present study, only one experienced observer recorded all colour Doppler images for off-line post-processing using dedicated software. Although we were particularly cautious to optimize the angle of the ultrasound beam, the velocity range settings and noise level, not all of the images were of optimal quality, and were therefore not analysed, especially for the assessment of radial strain and SR.

We had to discard 105 subjects from the analysis of radial strain, because of insufficient image quality, LV axis deviation (older subjects) and a thinner myocardial wall (younger subjects) often lead to non-perpendicular alignment of the ultrasound beam or artefacts due to endo- and epicardial reflection, respectively. These factors reduce the accuracy of the TDI technique in the assessment of the radial strain. Secondly, we estimated longitudinal strain and SR only from the basal segment of the inferior and inferolateral segments to avoid the problem of the inferior and inferolateral segments to avoid the problem of endo- and epicardial reflection, respectively. These factors reduce the accuracy of the TDI technique in the assessment of the radial strain. Secondly, we estimated longitudinal strain and SR only from the basal segment of the inferior and inferolateral LV free walls. We might therefore have underestimated the full spectrum of longitudinal deformation along the LV wall as well as between the LV walls. Whether the current proposed threshold values could be extrapolated to the anterior walls require further investigation. As shown in Supplementary material online, Table S1, in our healthy samples anterolateral strain was slightly lower than inferior and inferolateral strain with the opposite true for peak SR. However, fifth percentile of anterolateral strain (18.2%) fell within the 95% confidence boundaries of the fifth percentiles for longitudinal strain in the inferior walls, which ranged from 17.2 to 18.7%. Moreover, the major objective of our study was descriptive. We explored the early signs of LV systolic dysfunction in a general population, using the TDI technique. We would expect to detect early subclinical changes in systolic function in the LV basal segments, because the gradient of average wall stress increases from the apex to the base. For analysis, we averaged the inferior and inferolateral segments to avoid the problem of clustered observations in a single subject.

In conclusion, our study is the first to describe in a general population the distribution and determinants of LV strain and SR. We demonstrated that measurement of LV strain and SR is a sensitive tool in the detection of the subclinical systolic dysfunction associated with abdominal obesity and LV remodelling. Our current study resulted in the proposal for diagnostic thresholds for LV strain and SR, based on a healthy subgroup recruited via random sampling of the population.

Supplementary material
Supplementary material is available at European Heart Journal online.

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Optical coherence tomography assessment of vulnerable plaque rupture: predilection for the plaque ‘shoulder’

Peter Barlis, Patrick W. Serruys, Arie DeVries, and Evelyn Regar

Department of Cardiology, Thoraxcenter, Erasmus Medical Center Rotterdam, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands

* Corresponding author. Tel: +31 10 463 5729(E.R.), Fax: +31 10 463 5046(E.R.), E-mail: e.regar@erasusmc.nl (E.R.)

Atherosclerosis as a disease entity remains an intensely researched field, given the tendency for considerable morbidity and mortality. This attention has given rise to exciting opportunities in developing tools aimed at early detection and possible targeting of specific therapeutic interventions. One such modality is optical coherence tomography (OCT) that permits high-resolution visualization of backscattered light. This has given unique insights into disease processes and with greater detail than traditional grey scale intravascular ultrasound (IVUS). We present a 69-year-old man with 1 week crescendo angina 9 months following stent implantation to the left anterior descending (LAD) artery. Angiography demonstrated a new lesion in the mid LAD and diagonal branches. Assessment of the region with OCT revealed a high lipid content plaque with a thin fibrous cap (maximal thickness = 20 μm). In association, rupture of the thin cap was apparent, occurring at both shoulders of the plaque with associated mural thrombus. The patient was treated with further stent implantation and remains symptom-free at 3 months follow-up.

The predilection for plaque to rupture at the shoulder region is interesting. Pathological studies have shown that this region demonstrates intense inflammatory cell infiltrate, particularly with macrophage cells and lymphocytes. When activated, macrophages release matrix metalloproteinases in the vessel wall, which, in turn, can induce ‘weak spots’ that become susceptible to rupture. Other factors also implicated in this increased vulnerability at the plaque shoulder include neovascularization with expression of adhesion molecules and increased biomechanical stresses occurring around cellular microcalcifications within the thin cap.

Several imaging modalities have been used to assess and identify vulnerable plaque (VP) including coronary angioscopy, IVUS, and magnetic resonance imaging. Recently, there has been significant interest in the field of VP detection using OCT. This modality permits high-resolution imaging (10–20 μm), in the vicinity of 10 times greater than IVUS and has become a key tool to detect and quantify thin cap fibroatheroma and macrophage distribution. This individual clinical observation supports the evidence gained from post-mortem observations pointing to the plaque ‘shoulder’ as a site of vulnerability for rupture.

Panel A. Angiography in the right cranial view demonstrated stenosis in the mid left anterior descending artery involving both small diagonal branches. The previously proximally implanted left anterior descending artery stent was widely patent. The region corresponding to the optical coherence tomography images is shown with the black arrow.

Panel B–C. Intravascular optical coherence tomography (LightLab Imaging, Westford, MA, USA) was acquired using a non-occlusive technique with a 3.0 mm/s pullback. Optical coherence tomography clearly demonstrated the presence of a lipid-rich plaque in the 6–9 o clock position characterized by low reflectivity, speckled appearance with diffuse margins. This was covered with a bright rim of fibrous tissue corresponding to thin-cap fibroatheroma. Mural thrombus was evident in all optical coherence tomography cross sections. The thin-cap fibroatheroma measured was 20 μm thick, and was found to be ruptured at each of the two shoulders of the plaque (arrows).