Influence of Aging on Level and Layer-Specific Left Ventricular Longitudinal Strain in Subjects Without Structural Heart Disease

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Values for level- (apical, mid, and basal) and layer-based (endocardial, mid-myocardial, and epicardial) left ventricular (LV) longitudinal strain across age are scarce. The present study evaluates the effect of aging on level- and layer-specific LV longitudinal strain in subjects without structural heart disease. A total of 408 subjects (mean age 58 years [range 16 to 91]; 49% men) were evaluated retrospectively. Subjects were divided into equal groups based on age and gender. Subjects with evidence of structural heart disease or arrhythmias were excluded. Mean LV ejection fraction was $62 \pm 6.2\%$. A gradual increase in magnitude of level LV longitudinal strain was observed from basal to mid and apical levels ($-16.7 \pm 2.1\%$, $-18.8 \pm 2.0\%$, $-22.6 \pm 3.8\%$; p <0.001, respectively). Across age groups, there was a borderline significant decrease in magnitude of basal longitudinal strain in older subjects, whereas the magnitude in the apical level significantly increased. On layer-based analysis, the magnitude of longitudinal strain increased from epicardium to endocardium across all age groups. On multivariable analysis, only diabetes mellitus was associated with more impaired longitudinal strain in the endocardium, and male gender was associated with more impaired longitudinal strain at the epicardium layer. In conclusion, with increasing age, the magnitude of LV longitudinal strain at the basal level declines while the apical LV longitudinal strain increases. In contrast, layer-specific LV longitudinal strain remains unchanged with aging. The presence of diabetes mellitus modulated the effect of age on the LV endocardial layer, and male gender was associated with more impaired longitudinal strain at the epicardial layer. © 2017 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). (Am J Cardiol 2017;120:2065–2072)

Regional assessment of left ventricular (LV) longitudinal strain provides incremental prognostic value in ischemic heart failure patients.[1] Data from subjects without structural heart disease show a gradient in LV strain, with higher values in the apex compared with the basal segments.[2,3] In addition, the LV myocardium can be divided in 3 different layers (endocardial, mid-myocardial, and epicardial) that have a characteristic spatial disposition.[4] Whether the values of longitudinal strain in these different layers are similar or show variation in magnitude has not been evaluated in detail. In the present study, the influence of age on longitudinal strain (measured with 2-dimensional (2D) speckle tracking echocardiography) at 3 different LV levels (basal, mid, and apical) and 3 different LV layers (endocardium, mid-myocardium, and epicardium) was investigated in a large cohort of subjects without structural heart disease.

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Methods

Subjects who were clinically referred for transthoracic echocardiography at the Leiden University Medical Center (The Netherlands) between January 2005 and September 2016 were retrospectively evaluated. Subjects were referred for evaluation of dyspnea, syncope, chest pain, palpitations, preoperative screening before noncardiac surgery, or cardiac assessment due to high cardiovascular risk profile. Subjects with known history of coronary artery disease, LV wall motion abnormalities at rest, left ventricular ejection fraction (LVEF) <50%, previous cardiac surgery, pacemaker, arrhythmias or valvular heart disease (any grade of valve stenosis or more than mild valve regurgitation), congenital heart disease, or cardiomyopathies were excluded. Furthermore, subjects with suboptimal echocardiographic image quality precluding reliable speckle tracking analysis were excluded. A total of 408 subjects were included and divided into approximately equally distributed groups based on age and gender. Five age categories were defined: <45 years, 45 to 54 years, 55 to 64 years, 65 to 74 years, and >75 years.[3] To reflect a real-world aging population, subjects with cardiovascular risk factors (hypertension, smoking status, diabetes mellitus, dyslipidemia, and family history of coronary artery disease) were not excluded.

Demographics and clinical characteristics were recorded. All clinical data were stored at the departmental Cardiology

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Information System (EZIS chipsoft and EPD-Vision, Leiden University Medical Center, Leiden, The Netherlands) and retrospectively analyzed. The Dutch Central Committee on Human-related Research (CCMO) allows the use of anonymous data without previous approval of an institutional review board provided that the data are acquired for routine patient care. All data used for this study were acquired for clinical purposes and handled anonymously.

Images were obtained with subjects at rest in the left lateral decubitus position using commercially available ultrasound systems (Vivid 7 and E9, General Electric Vingmed, Horten, Norway). Data acquisition was performed with a 3.5-MHz or M5S transducers. Standard M-mode, 2D, color, and pulsed and continuous wave Doppler images were acquired and stored digitally for subsequent offline analysis (EchoPac BT13, GE Medical Systems, Horten, Norway). LVEF was calculated using the Simpson's biplane method of discs according to current recommendations.[5] LV mass was calculated according Devereux et al, and indexed for body surface area.[5] Valvular morphology and function were assessed with 2D, color, and pulsed and continuous wave Doppler echocardiography.[6] Left ventricular diastolic function was assessed by measuring the peak early (E) and late (A) diastolic velocities on transmitral flow pulsed-wave recordings. The average of E' septal and E' lateral measured in the apical 4-chamber view on tissue Doppler imaging was used for this analysis.[7] Right ventricular (RV) function was evaluated according to current recommendations by measuring the tricuspid annular plane systolic excursion in the apical 4-chamber view using the M-mode.[8] Systolic pulmonary artery pressure was estimated by adding the RV pressure to right atrial pressure. The RV pressure was estimated by calculating the systolic pressure gradient between the RV and right atrium by the peak velocity of the regurgitant jet of the tricuspid valve (if present) using the modified Bernoulli equation.[8] Right atrial pressure was estimated by measuring the diameter and the inspiratory collapse of the inferior vena cava.[8]

From the apical 4-, 2-, and long-axis views, 2D speckle tracking echocardiography was applied to analyze longitudinal strain at 3 different LV levels (apex, mid, basal) and 3 different LV layers (endocardial, mid-myocardial, and epicardial). The endocardial border was manually traced at end-systole and the region of interest including the entire LV myocardial wall was displayed.[9] The software automatically tracks and accepts segments of good tracking quality and rejects poorly tracked segments while allowing the observer to manually override its decisions based on visual assessment of tracking quality. Global LV longitudinal strain was obtained as the average of longitudinal strain of 17 segments (Figure 1). Subsequently, longitudinal strain values of the apex, mid, and basal levels of the LV were obtained by averaging the value of strain of the 5 apical segments and the 6 basal and 6 mid-ventricular segments (Figure 2). Finally, the software allows for analysis of the LV longitudinal strain of the 3 different layers: endomyocardial, mid-myocardial, and epicardial. Layer-specific longitudinal strain values are obtained as the average of longitudinal strain of 17 segments at each layer (Figure 3). The mid-myocardial strain is the average of the epicardial and endocardial layers.

Continuous variables are reported as mean ± standard deviation for normally distributed variables and were analyzed using one-way analysis of variance. Categorical variables are reported as frequencies and percentages and were analyzed
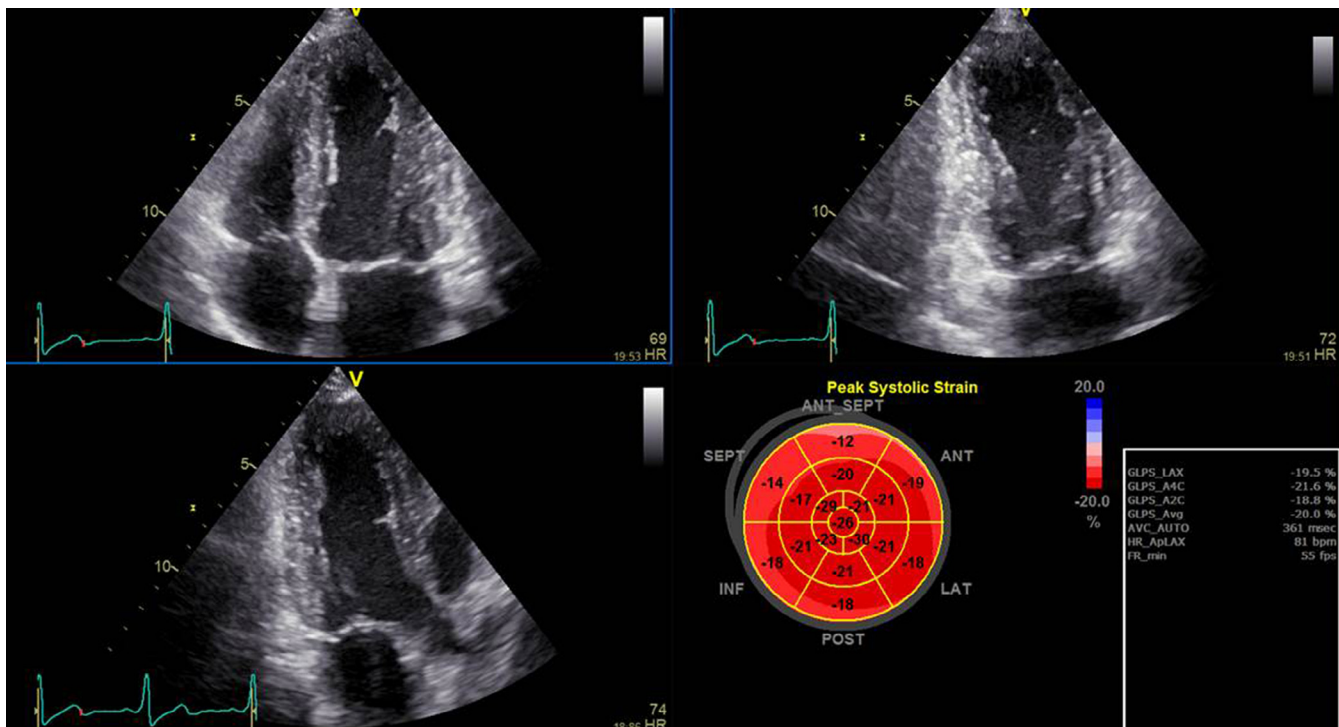

Figure 1. Global left ventricular longitudinal strain assessment. From the apical 4-, 2-, and long-axis views the global longitudinal strain value is calculated. ANT = anterior; ANT_SEPT = anterior-septal; INF = inferior; LAT = lateral; POST = posterior; SEPT = septal.
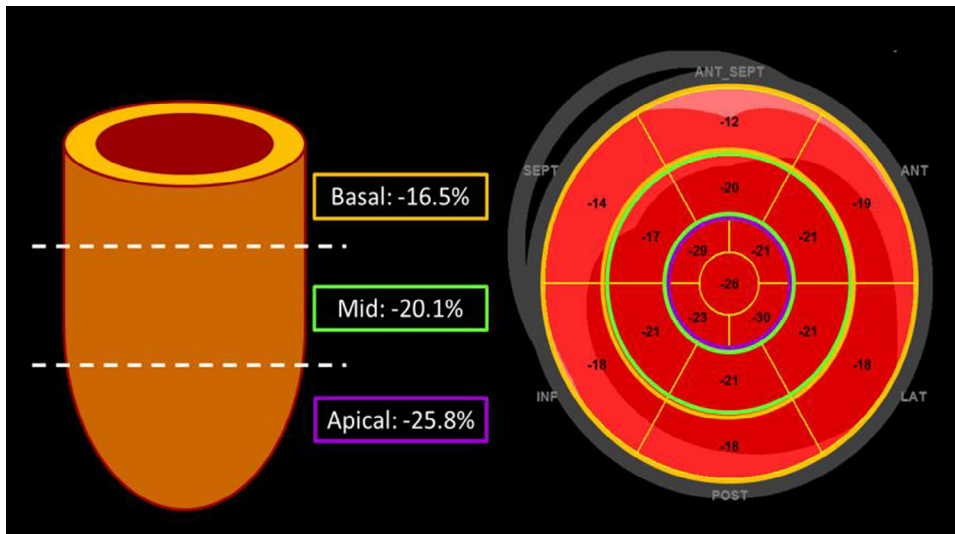
Figure 2. Longitudinal strain per level: apex, mid, and basal. Left ventricular longitudinal strain at the basal (orange), mid-ventricular (green), and apical (purple) levels are calculated as the average of the regional values. ANT = anterior; ANT_SEPT = anterior-septal; INF = inferior; LAT = lateral; POST = posterior; SEPT = septal.
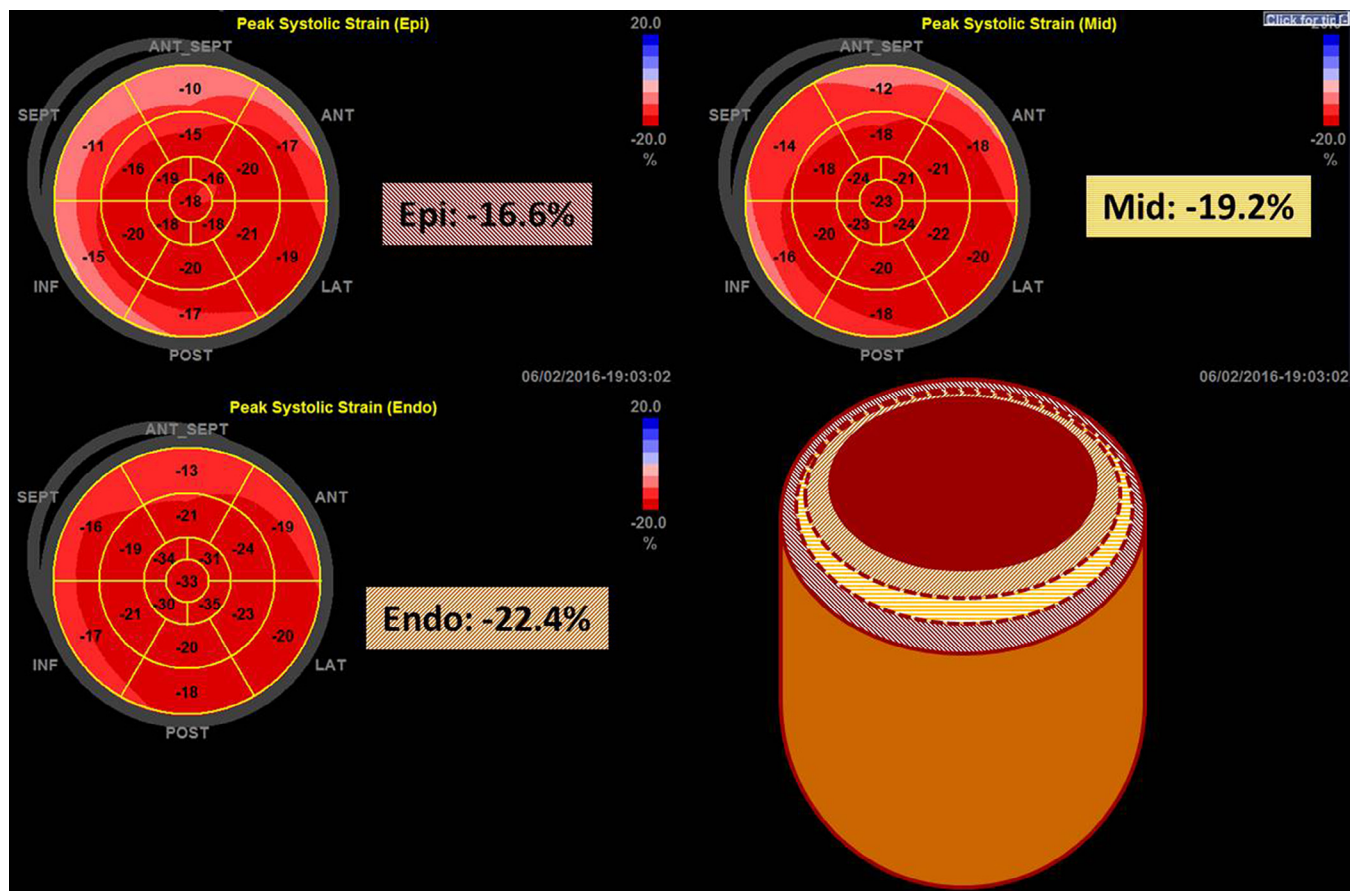

Figure 3. Layer-specific longitudinal strain analysis. The bull-eye's plots for the endocardium, mid-myocardium, and epicardium are displayed, and the global value of longitudinal strain at each layer is calculated as the average of the 17 regional strain values per layer. ANT = anterior; ANT_SEPT = anterior-septal; INF = inferior; LAT = lateral; POST = posterior; SEPT = septal.

using the chi-square test. Comparison of LV longitudinal strain of the 3 myocardial levels (basal, mid-ventricular, and apical) and the 3 myocardial layers (endocardial, mid-myocardial, and epicardial) across age categories was performed using a linear mixed model for hierarchical data. The age category was incorporated into the model as fixed variable as well as the interaction between age and LV longitudinal strain. A diagonal covariance matrix was applied for repeated effects.

The estimated marginal means and standard deviation of numerical data are presented. Pairwise comparisons were performed to assess differences between age categories. Univariate and multivariable analysis was performed to examine the effect of age on layer-specific longitudinal systolic strain, adjusted for known confounders such as traditional risk factors and cardiovascular medications. Level of significance for univariate analysis was set at p <0.20. The intraclass correlation coefficient (ICC) was calculated to assess the inter- and intraobserver variability for global longitudinal strain (GLS). Twenty randomly selected subjects were analyzed by 2 separate readers. An excellent agreement was defined as ICC >0.75, whereas strong agreement was defined as ICC 0.60 to 0.74. Statistical analysis was performed on SPSS for Windows v20.0 (IBM, Armonk, New York). A 2-tailed p-value of <0.05 was considered statistically significant.

Results

Global, level-, and layer-specific values of LV longitudinal strain were compared between subjects with versus subjects without cardiovascular risk factors or medications (Table 1). There were no statistically significant differences in LV GLS, level-, and layer-specific longitudinal strain between groups and, accordingly, we investigated the effects of aging in the overall population.

The clinical characteristics of the subjects classified according to 5 age categories are presented in Table 2. There was a significant increase in the prevalence of hypertension, hypercholesterolemia, and type II diabetes mellitus across the age categories, whereas family history of cardiovascular disease was more prevalent among younger and middle-age groups (Table 2). The use of cardiovascular medications was more frequently noted in older groups (Table 2).

There were no significant differences in LVEF and LV GLS across the different age groups (Table 3). Furthermore, subjects showed more impaired diastolic function with

Table 1
Characteristics for subjects without versus with cardiovascular risk factors

Variable	Cardiovascular risk factors		
	No (n = 94)	Yes (n = 314)	p-value
Age (years)	54 ± 16	59 ± 16	0.004
Men	54 (57%)	145 (46%)	0.055
BSA (m²)	1.9 ± 0.2	1.9 ± 0.2	0.709
BMI (kg/ m²)	25 ± 3.4	26 ± 4.2	0.139
Cardiovascular risk factors	0	314 (100%)	<0.001
Medication	0	181 (58%)	<0.001
Global longitudinal strain	−19.2 ± 2.0	−18.8 ± 2.0	0.072
Basal	−16.9 ± 2.4	−16.7 ± 2.1	0.528
Mid	−18.9 ± 2.1	−18.8 ± 2.0	0.630
Apical	−22.8 ± 4.0	−22.6 ± 3.7	0.485
Endocardium	−21.8 ± 2.4	−22.2 ± 2.3	0.126
Mid-myocardium	−19.3 ± 2.3	−19.0 ± 2.0	0.297
Epicardium	−17.0 ± 1.8	−16.6 ± 1.9	0.051

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; BSA = body surface area.

Data are presented as mean ± standard deviation or as number (percentage).

Hypertension was defined as office blood pressure ≥140/90 mm Hg or previous pharmacological treatment. Hypercholesterolemia was defined as total cholesterol 190 mg/dl or previous pharmacological treatment. Diabetes mellitus was defined as fasting blood glucose ≥7.0 mmol/L, 2-h oral glucose tolerance test glucose ≥11.1 mmol/L, previous pharmacological treatment.

Table 2
Clinical characteristics according to age category

Variable	Age category (years)					
	<45 (n = 86)	45–54 (n = 82)	55–64 (n = 83)	65–74 (n = 80)	>75 (n = 77)	p-value
Age (years)	34 ± 8	50 ± 3	59 ± 3	69 ± 3	80 ± 4	—
Men	45 (52%)	42 (51%)	40 (48%)	40 (50%)	32 (42%)	0.682
BSA (m²)	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	0.118
BMI (kg/ m²)	25 ± 3	25 ± 4	26 ± 6	26 ± 4	26 ± 4	0.061
Hypertension	14 (16%)	20 (25%)	27 (33%)	38 (48%)	48 (64%)	<0.001
Hypercholesterolemia	3 (4%)	11 (14%)	17 (21%)	22 (28%)	19 (25%)	<0.001
Diabetes mellitus I	0 (0%)	2 (3%)	3 (4%)	2 (3%)	1 (1%)	0.508
Diabetes mellitus II	1 (1%)	9 (11%)	8 (10%)	12 (15%)	5 (7%)	0.023
Smoker	9 (12%)	11 (17%)	7 (11%)	3 (6%)	5 (9%)	0.395
Family history CVD	36 (42%)	34 (43%)	27 (33%)	17 (22%)	19 (27%)	0.021
ACEi	6 (7%)	9 (11%)	10 (12%)	19 (24%)	12 (16%)	0.028
ARB	3 (4%)	7 (9%)	9 (11%)	10 (13%)	14 (19%)	0.033
Beta-blocker	7 (8%)	6 (10%)	12 (15%)	19 (24%)	17 (23%)	0.013
Calcium-channel blocker	5 (6%)	6 (8%)	7 (9%)	8 (10%)	12 (16%)	0.219
Statins	3 (4%)	11 (14%)	20 (24%)	22 (28%)	20 (27%)	<0.001
Diuretics	7 (8%)	10 (13%)	6 (7%)	14 (18%)	26 (35%)	<0.001
Insulin therapy	1 (1%)	4 (5%)	6 (7%)	4 (5%)	2 (3%)	0.328

ACEi = angiotensin-converting enzyme inhibitor, ARB = angiotensin II receptor blocker, BMI = body mass index, BSA = body surface area, CVD = cardiovascular disease.

Data are presented as mean ± standard deviation or as number (percentage).

Hypertension was defined as office blood pressure ≥140/90 mm Hg or previous pharmacological treatment. Hypercholesterolemia was defined as total cholesterol 190 mg/dl or previous pharmacological treatment. Diabetes mellitus was defined as fasting blood glucose ≥7.0 mmol/L, 2-h oral glucose tolerance test glucose ≥11.1 mmol/L, previous pharmacological treatment.

Table 3
Echocardiographic characteristics according to age category

Variable	Age category (years)					
	<45 (n = 86)	45–54 (n = 82)	55–64 (n = 83)	65–74 (n = 80)	>75 (n = 77)	p-value
Heart rate (bpm)	72 ± 14	72 ± 13	67 ± 11	72 ± 12	71 ± 11	0.037
Interventricular septum (mm)	9.6 ± 1.7	9.8 ± 1.6	10.3 ± 1.5	10.2 ± 2.0	10.6 ± 1.7	0.004
LV end-diastolic diameter (mm)	48 ± 5	48 ± 7	48 ± 6	49 ± 7	46 ± 9	0.017
LV end-systolic diameter (mm)	31 ± 6	30 ± 5	31 ± 7	32 ± 7	29 ± 5	0.895
LV posterior wall diameter (mm)	10 ± 3	10 ± 2	10 ± 3	10 ± 2	10 ± 1	0.900
LV mass, indexed (g/m^2)	87 ± 19	89 ± 22	93 ± 21	96 ± 24	94 ± 20	0.030
Aortic diameter (mm)	31 ± 4	32 ± 4	34 ± 4	34 ± 4	34 ± 3	<0.001
LA diameter (mm)	34 ± 4	35 ± 5	36 ± 6	36 ± 5	37 ± 6	0.015
LA indexed volume (ml/m^2)	23 ± 7	22 ± 7	25 ± 7	24 ± 9	24 ± 7	0.182
LV end-diastolic volume (ml)	114 ± 28	105 ± 28	108 ± 28	99 ± 27	91 ± 23	<0.001
LV end-systolic volume (ml)	47 ± 18	42 ± 16	44 ± 16	38 ± 15	34 ± 12	<0.001
LV ejection fraction (%)	61 ± 6	62 ± 6	61 ± 6	63 ± 6	63 ± 6	0.077
Global longitudinal strain (%)	−18.8 ± 2.0	−19.0 ± 2.0	−19.0 ± 2.0	−18.7 ± 2.0	−19.0 ± 2.0	0.722
E/A ratio	1.4 ± 0.4	1.2 ± 0.3	1.1 ± 0.3	0.9 ± 0.3	0.9 ± 0.4	0.090
E' (cm/s)	16.3 ± 3.4	13.2 ± 3.2	11.9 ± 2.4	9.7 ± 2.6	8.7 ± 3.0	<0.001
E/E'	4.9 ± 1.2	5.8 ± 2.3	6.2 ± 1.5	8.1 ± 7.6	8.9 ± 4.3	<0.001
TAPSE	24 ± 4.2	24 ± 4.0	24 ± 3.6	25 ± 4.0	24 ± 4.0	0.558
Systolic PAP	24 ± 5.3	25 ± 6.3	25 ± 6.0	25 ± 6.0	26 ± 5.6	0.253

LA = left atrial, LV = Left ventricular, PAP = pulmonary pressure, TAPSE = tricuspid annular plane systolic excursion.
Data are presented as mean ± standard deviation.

increasing age (Table 3). At LV level-based analysis (basal, mid-ventricular, and apical), an increasing gradient in magnitude of longitudinal strain from the basal to mid and apical levels was observed for the entire population: the apical level showed the highest magnitude of strain (−22.6 ± 3.8%), whereas the basal level showed the lowest strain (−16.7 ± 1.9%) (Table 4). The individual predetermined age categories showed the same trend with an increasing gradient in magnitude of longitudinal strain from the basal to mid and apical levels (p <0.001 for all groups). Interestingly, a subtle decrease in the magnitude of longitudinal strain at the basal level was observed from younger to older age categories (p = 0.052). However, we did observe an increase in the magnitude of longitudinal strain at the apical level (p <0.001) (Table 4). There was no significant difference across categories in peak systolic strain at the mid-ventricular level (p = 0.179).

Layer-specific analysis (endocardium, mid-myocardium, and epicardium) showed a decrease in magnitude of longitudinal strain from endocardium to mid-myocardium and epicardium for the overall population and all individual age categories (p <0.001 for all groups; Table 5). This trend did

not differ across the various age categories (endocardium, p = 0.371; mid, p = 0.140; epicardium, p = 0.493).

On univariate analysis, increasing age was not associated with peak systolic strain at the endocardial (β = −0.028, p = 0.572), mid-myocardial layer (β = −0.046, p = 0.357), or the epicardial layer (β = −0.063, p = 0.206). In addition, hypercholesterolemia, smoking, heart rate, calcium channel blockers, and LV mass (indexed) were not associated with longitudinal strain at all layers. Therefore, these variables were not forced into the multivariate analysis. On multivariable analysis, diabetes mellitus was associated with more impaired longitudinal strain in the endocardium (β = 0.103, p = 0.040), and male gender was associated with more impaired longitudinal strain at the epicardium (β = −0.116, p = 0.018) (Table 6). The effect of age on layer-specific peak systolic strain, corrected for these variables (gender, diabetes mellitus), is demonstrated in Figure 4. There were no significant differences in global peak systolic strain across the age categories for the endocardium (p = 0.785), mid-myocardium (p = 0.494), and epicardium (p = 0.283).

Intra- and interobserver reproducibility for GLS measurements were excellent with an ICC of 0.816 (95% confidence

Table 4
Level specific peak systolic left ventricular longitudinal strain divided by age categories

Age categories (years)						
Myocardial level	<45 (n = 86)	45–54 (n = 82)	55–64 (n = 83)	65–74 (n = 80)	>75 (n = 77)	Overall (n = 408)
Basal	−17.1 ± 2.3	−16.9 ± 2.1	−16.7 ± 2.3	−16.8 ± 2.0	−16.1 ± 2.1	−16.7 ± 2.2
Mid	−18.8 ± 2.0	−19.1 ± 2.4	−19.0 ± 1.8	−18.9 ± 1.9	−18.4 ± 2.1	−18.8 ± 2.0
Apical	−21.6 ± 3.3	−22.2 ± 3.6	−22.9 ± 3.4	−23.4 ± 4.3	−23.1 ± 4.0	−22.6 ± 3.8
*p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Data are presented as mean ± standard deviation.
* p-value for level specific outcome (referenced to apical).

Table 5

Layer specific global peak systolic left ventricular longitudinal strain divided by age categories

Age categories (years)						
Myocardial layer	<45 (n = 86)	45–54 (n = 82)	55–64 (n = 83)	65–74 (n = 80)	>75 (n = 77)	Overall (n = 408)
Endocardium	−21.9 ± 2.3	−22.1 ± 2.5	−22.2 ± 2.1	−22.5 ± 2.5	−22.1 ± 2.4	−22.1 ± 2.4
Mid-myocardium	−18.1 ± 2.0	−19.1 ± 2.2	−19.3 ± 1.7	−19.5 ± 2.1	−18.8 ± 2.2	−19.1 ± 2.1
Epicardium	−16.4 ± 1.8	−16.8 ± 2.3	−16.8 ± 1.7	−16.8 ± 1.7	−16.6 ± 1.9	−16.7 ± 1.9
***p-value**	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Data are presented as mean ± standard deviation.

* p-value for layer specific outcome (referenced to epicardium).

Table 6

Independent correlates for layer specific peak systolic left ventricular longitudinal strain

Variable	Endocardial				Mid-myocardial				Epicardium			
	Univariate		Multivariate		Univariate		Mutlivariate		Univariate		Multivariate	
	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value
Gender (female)	−0.072	0.144	−0.074	0.137	−0.079	0.113	−0.088	0.078	−0.108	0.029	−0.116	0.018
Hypertension	0.024	0.635	—	—	0.112	0.024	0.063	0.310	0.145	0.004	0.075	0.227
Diabetes mellitus	0.095	0.057	0.103	0.040	0.108	0.031	0.086	0.090	0.101	0.042	0.070	0.161
ACEi/ARBS	0.059	0.235	—	—	0.125	0.012	0.066	0.292	0.172	0.001	0.108	0.083
Beta-blocker	−0.81	0.105	−0.082	0.100	−0.039	0.440	—	—	−0.033	0.514	—	—

ACEi = angiotensin-converting enzyme inhibitor, ARB = angiotensin II receptor blocker, LV = left ventricular.
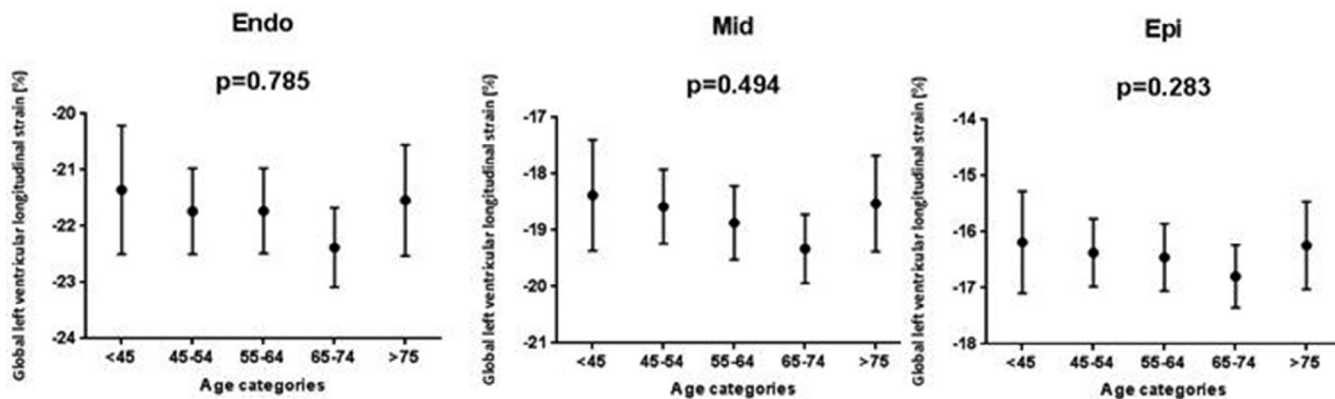

Figure 4. Layer-specific left ventricular longitudinal strain across age categories. Means and 95% confidence intervals for layer-specific global longitudinal strain (endocardial, mid-myocardial, and epicardial layers) across the predetermined age categories (x axis) are displayed. There were no significant differences in global peak systolic strain across the age categories after adjusting for gender and diabetes mellitus in a linear mixed model. endo = endocardium; epi = epicardium; mid = mid-myocardial.

interval 0.487 to 0.930) and an interclass correlation coefficient of 0.772 (95% confidence interval 0.437 to 0.909).

Discussion

Although data on global LV longitudinal strain are accumulating in healthy volunteers and subjects without structural or functional heart disease, data on level- and layer-specific longitudinal strain are scarce.[2,3,10] A recent meta-analysis of 24 studies totaling 2,597 subjects without structural heart disease (mean age 47 ± 11 years, 51% men) reported that the normal values of global LV longitudinal strain ranged from −15.9% to −22.1%.[11] Clinical characteristics of the included subjects and the vendor-specific software used to analyze longitudinal strain may explain the disparate values of global LV longitudinal strain. In the present study, the mean value of global LV longitudinal strain for the overall population was −18.9% and did not differ significantly across the different age categories.

In terms of level-specific LV longitudinal strain, previous studies have shown a gradient in longitudinal strain from the base to the apex, showing the basal segments a smaller magnitude of longitudinal strain compared with the apical segments.[2,3,12] During systole, wall stress decreases toward the apex due to smaller circumferential radius of curvature which leads to higher magnitude of longitudinal strain in the apex

compared with the base.[13] Furthermore, this gradient can be also explained by the different composition of the myocardium with more cross-fiber shortening in the apex compared with the LV base.[13]

However, changes in the gradient across different age categories in a real-world aging population have not been studied so far. The present study shows that the gradient in longitudinal strain from base to apex is kept constant across the age categories. Interestingly, aging was associated with a borderline significant decline in LV longitudinal strain magnitude in the basal segments and significant enhancement of longitudinal strain magnitude in apical segments. Aging is known to be associated with fibrotic remodeling of the LV while having preserved function and contractility.[14] The increase of interstitial fibrosis and LV mass leads to increased stiffness of the LV myocardium and impaired diastolic relaxation as demonstrated in our study. To maintain low LV filling pressures, the LV shows an increase of the longitudinal strain in the apical segments during systole as a compensatory mechanism.[15]

To further explore the effect of aging on LV mechanics, the present study evaluated the layer-specific longitudinal strain (from endocardium to epicardium). The larger magnitude of longitudinal strain in the endocardium compared with the epicardium can be explained by the larger end-diastolic wall stress in the endocardium which leads to larger fiber stretch at end-diastole and larger shortening during systole.[13] Layer-specific longitudinal strain analysis is increasingly being used in the detection of global and regional LV dysfunction.[16,17] Previous study reported the layer-specific values of longitudinal strain in a single center study including 119 healthy volunteers (age range, 22 to 76 years; 50% women).[10] A gradient from the endocardium to the epicardium was observed with the highest magnitude of longitudinal strain in the endocardial layer ($-24.3 \pm 3.1\%$) and the lowest in the epicardial layer ($-18.9 \pm 2.8\%$). Compared with men, women showed slightly more preserved values of longitudinal strain at all the layers. Similar to our study, aging did not influence significantly on layer-specific longitudinal strain values.

Several factors may influence global LV longitudinal strain in subjects without structural heart disease. Diabetes and hypertension for example have been associated with impaired global LV longitudinal strain.[18,19] However, little is known about the correlates of LV layer-specific GLS. Other studies have shown that hypertension has an important influence on layer-specific longitudinal strain. In 145 subjects with hypertension and preserved LVEF, Kim et al showed that longitudinal strain was significantly reduced (less negative) in all the myocardial layers compared with 31 normotensive controls.[20] Importantly, LV mass was strongly associated with layer-specific longitudinal strain, and those subjects with larger LV mass showed more impaired longitudinal strain across all the myocardial layers. The present study showed that diabetes was associated with impaired longitudinal strain of the endocardial layer. This is in line with previous studies showing that the endocardium is most susceptible to early injury caused by diabetes.[21,22] In addition, impaired longitudinal strain of the endocardial layer has been associated with cardiovascular events in patients with coronary artery disease.[16,23] Whether this may be extended to subjects with cardiovascular risk factors needs further research.

Several limitations should be acknowledged. The current study was retrospective and included subjects without structural heart disease but a significantly high prevalence of cardiovascular risk factors that may influence LV mechanics. Therefore, the values of level- and layer-specific longitudinal strain reported in this article may not be generalizable. Blood pressure values and complications of diabetes mellitus were not systematically available. Furthermore, LV strain measurements were performed with dedicated postprocessing software, and the values obtained with this specific software may not be generalized to other vendors.

In conclusion, with increasing age, the magnitude of LV longitudinal strain at the basal level decreases, whereas the apical LV longitudinal strain increases. In contrast, layer-specific LV longitudinal strain remains unchanged with aging. The presence of diabetes mellitus modulated the effect of age on the LV endocardial layer, and male gender was associated with more impaired longitudinal strain at the epicardial layer.

Disclosures

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