Tissue Doppler indexes of left ventricular systolic function in relation to the pulsatile and steady components of blood pressure in a general population

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Objectives: To our knowledge, no population study described the association of the radial and longitudinal components of left ventricular strain with blood pressure (BP) components in continuous analyses. We therefore investigated these associations in participants randomly recruited from the general population in the framework of the family-based European Project on Genes in Hypertension.

Methods: In 334 participants (55.4% women; mean age, 43.6 year), using tissue Doppler imaging (TDI), we measured the end-systolic longitudinal strain (mean 20.9%) and peak systolic strain rate (1.29 s^{-1}) from the basal portion of the left ventricular inferior and posterior free walls and radial strain (51.1%) and strain rate (3.40 s^{-1}) of the left ventricular posterior wall. Models included in addition to covariables and confounders both SBP and DBP or both pulse pressure (PP) and mean arterial pressure (MAP). Effect sizes were expressed per 1-SD increase in BP.

Results: Longitudinal strain (-0.62% ; $P=0.04$ and -0.64% ; $P=0.007$), but not strain rate, decreased with DBP and MAP. Radial strain (4.0 and -3.4% ; $P\leq 0.001$) and strain rate (0.38 and -0.18 s^{-1} ; $P\leq 0.04$) independently increased with SBP and decreased with DBP. Accordingly, radial strain (2.9% ; $P<0.0001$) and strain rate (0.22 s^{-1} ; $P=0.0005$) increased with higher PP, but were not related to MAP.

Conclusion: In the general population, BP is an independent determinant of left ventricular systolic function as measured by TDI. Radial function increased with PP, the pulsatile BP component, whereas longitudinal function decreased with the steady component of BP as expressed by MAP or DBP.

Keywords: blood pressure, left ventricular function, population, strain

Abbreviations: BP, blood pressure; EPOGH, European Project on Genes in Hypertension; MAP, mean arterial pressure; PP, pulse pressure; RWT, relative wall thickness; SPEQLE, Software Package For Echocardiographic

Quantification LEuven; TDI, tissue Doppler imaging; VIF, variance inflation factor; WHR, waist-to-hip ratio

INTRODUCTION

Age-related stiffening of the large arteries leads to an increase in SBP. The heart typically adapts to confront higher earlier and later systolic loads by both hypertrophy and left ventricular stiffening. Hypertensive patients usually present with concentric remodeling or concentric left ventricular hypertrophy, but have a normal-sized left ventricular chamber and normal or even slightly enhanced ejection fraction. However, previous studies in hypertensive patients showed a reduced left ventricular longitudinal and midwall fractional shortening as measured by echocardiography [1–5] or MRI [6]. Thus, ejection fraction, which reflects only left ventricular cavity emptying, may be insensitive to detect early impairment of systolic function in response to an increased afterload. Using modern echocardiographic techniques, such as tissue Doppler imaging (TDI) or speckle tracking, one can evaluate how the functional adaptation of the left ventricle to increased cardiac load differs among patients. On the basis of color Doppler myocardial imaging, one-dimensional regional longitudinal and radial strain and

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strain rate curves can be calculated by comparing local myocardial velocity profiles [7]. To our knowledge, no population study described the association of the radial and longitudinal left ventricular strain with different blood pressure (BP) components in continuous analyses. We therefore investigated these associations in patients recruited from general population in the framework of the family-based European Project on Genes in Hypertension (EPOGH).

METHODS

Study participants

EPOGH was conducted according to the principles outlined in the Helsinki declaration for investigations in humans [8]. The Ethics Committee of each institution approved the protocol. Participants provided informed consent. Three EPOGH centers opted to take part in the echocardiographic substudy. They randomly recruited nuclear families from the general population, including offspring with a minimum age of 18 years. Overall, the response rate was 61.3% [9].

Our study population consisted of 370 individuals, who in 2006–2008 underwent the echocardiographic examination in Gdansk ($n=112$) and Cracow ($n=148$), Poland, and Novosibirsk, the Russian Federation ($n=110$). We excluded 14 individuals from statistical analysis, because of myocardial infarction or coronary revascularization ($n=3$), because of moderate-to-severe valvular abnormalities ($n=7$), or because of atrial fibrillation ($n=4$). Because the color Doppler myocardial images were of insufficient quality, we additionally discarded 22 individuals from the analysis of left ventricular longitudinal strain and 52 individuals from the analysis of left ventricular radial strain, leaving 334 and 304 participants, respectively.

Echocardiography

The participants refrained from smoking, heavy exercise, and drinking alcohol or caffeine-containing beverages for at least 3 h before echocardiography.

Data acquisition

In each center, one experienced physician (W.S., M.L., A.R.) did the ultrasound examination, using a Vivid7 Pro (GE Vingmed, Horten, Norway) interfaced with a 2.5–3.5-MHz phased-array probe, according to a standardized protocol as previously described [10]. With the individuals 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 left ventricle were recorded from the parasternal long-axis view under control of the two-dimensional 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 frames/s) 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 to avoid aliasing.

Off-line analysis

Digitally stored images were transferred to the Coordinating Center in Leuven for further postprocessing. One experienced observer analyzed the echocardiographic images, using a workstation running the EchoPac, version 4.0.4 (GE Vingmed) software package. We averaged three heart cycles for statistical analysis. The left ventricular internal diameter and interventricular septal and posterior wall thickness were measured at end diastole from the two-dimensionally guided M-mode tracing, as described in the American Society of Echocardiography guideline [11]. End-diastolic left ventricular dimensions were used to calculate left ventricular mass by an anatomically validated formula. Relative wall thickness (RWT) was calculated as the ratio of (interventricular septum + posterior wall thickness)/left ventricular internal diameter at end diastole. Left ventricular end-systolic and end-diastolic volumes and ejection fraction were calculated using Teicholtz's method.

We extracted strain and strain rate curves off-line from color tissue Doppler images, using research-dedicated software as previously described [10]. The SPEQLE software (version 4.6.2, University of Leuven, Belgium) 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. Moreover, it also allows the accurate implementation of timing of global mechanical events into the deformation curves. We positioned the sampling volume in the basal portion of the interrogated wall at the level of the posterior chordae tendineae. To compute end-systolic strain and peak systolic strain rate, from now on referred to as strain and strain rate, we averaged three consecutive cycles. We calculated the radial strain rate of the posterior wall and the longitudinal strain rate of the inferior and posterior walls, by measuring the spatial velocity gradient over a computation area of 5 and 10 mm, respectively. Strain profiles were obtained by integrating the mean strain rate profile over time [7]. 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 three to five beams per pixel. Because there were no differences between the posterior and inferior walls in longitudinal strain and strain rate, for statistical analysis, we averaged these measurements and used their absolute values.

As reported previously [10], the interobserver reproducibility was 15.8 and 18.3% for longitudinal and radial strain and 16.7–14.0% for longitudinal and radial strain rate, respectively.

Blood pressure measurements

Trained observers measured BP with a standard mercury sphygmomanometer five times consecutively at the examination center. Standard cuffs had a 12 cm $\times$ 24 cm inflatable bladder, but, if upper arm circumference exceeded 31 cm, larger cuffs with a 15 cm $\times$ 35 cm bladder were used. After at least 10 min rest, five consecutive BP readings were

obtained in the sitting position with an interval of 30–60 s between readings. The cuff was deflated at approximately 2 mmHg/s, and SBP and phase V DBP were recorded to the nearest 2 mmHg. Hypertension was defined as a BP of at least 140 mmHg systolic or 90 mmHg diastolic or as the use of antihypertensive drugs. Pulse pressure (PP) was SBP–DBP. Mean arterial pressure (MAP) was DBP plus one-third of PP.

Other measurements

We administered a standardized questionnaire to collect detailed information on each participant's medical history, smoking and drinking habits, and intake of medications. BMI was weight in kilograms divided by the square of height in meters. Waist and hip circumferences were measured to the nearest centimeter with a tape measure while the individual was standing.

Statistical methods

For database management and statistical analysis, we used SAS software, version 9.2 (SAS Institute, Cary, North Carolina, USA). The central tendency and the spread of the data are reported as mean $\pm$ SD. We compared means and proportions by means of a large sample z -test and by the χ^2 -test, respectively. Significance was P less than 0.05 on two-sided test. While accounting for center, we performed stepwise multiple regression to assess the independent correlations of strain and strain rate with sex, age, anthropometric characteristics [height, weight, BMI, waist circumference, and waist-to-hip ratio (WHR)] and heart rate. We set the P values for variables to enter and to stay in the regression models at 0.10. Next, we tested the multi-variable-adjusted associations between left ventricular systolic function indexes and BP components using a mixed model. This technique allows accounting for covariables as well as for the nonindependence of observations within families. The indexes of left ventricular function and the BP

components were analyzed as continuous variables. We ran regression diagnostics to exclude the possibility that collinearity inappropriately influenced our multivariable models. In linear regression, we computed the variance inflation factor (VIF). In single BP component models, VIFs were less than 2.00 for all explanatory variables including BP component (models 1, 2, 4, and 5) with the exception of VIF for the WHR in relation to longitudinal velocity (VIF = 2.51). In multiple regression models, which included simultaneously two BPs components (models 3 and 6), VIF were 2.86 and 2.62 for SBP and DBP, and 1.48 and 1.84 for PP and MAP, respectively.

RESULTS

Characteristics of participants

The 334 participants included 185 (55.4%) women and 157 (47.0%) hypertensive patients, 92 (27.5%) of whom were on antihypertensive drug treatment. Tables 1 and 2, respectively, show the clinical and echocardiographic characteristics of the participants by generation and sex. The mean age of the parents and offspring ($\pm$ SD) was 57.4 ± 7.6 and 30.4 ± 6.7 years, respectively. In comparison with offspring, parents had higher BMI, WHR, BP, and more frequently reported use of antihypertensive drugs ($P < 0.0001$ for all comparisons). The echocardiographic measurements reflecting left ventricular wall thickness and left ventricular mass index (Table 2) were greater in men than in women in both generations. In the parent generation, ejection fraction was greater in women in comparison with men ($P = 0.0007$).

Systolic strain, strain rate, and velocity

In all participants, strain averaged 20.9% [95% confidence interval (CI) 15.5–26.7] longitudinal and 51.1% (95% CI 32.5–68.8%) radial. Strain rate averaged 1.29 s^{-1} (0.89– 1.85 s^{-1}) longitudinal and 3.40 s^{-1} (1.94 – 5.18 s^{-1}) radial.

TABLE 1. General characteristics by generation and sex

Characteristic	Parents		P	Offspring		P
	Women (n = 97)	Men (n = 66)		Women (n = 88)	Men (n = 83)	
Anthropometrics						
Age (years, mean ± SD)	57.1 ± 7.7	57.9 ± 7.6	0.52	30.8 ± 7.5	29.9 ± 6.7	0.40
Weight (kg, mean ± SD)	75.9 ± 14.4	86.4 ± 14.1	<0.0001	64.9 ± 14.5	84.5 ± 16.0	<0.0001
Height (cm, mean ± SD)	160.1 ± 5.4	172.4 ± 6.0	<0.0001	165.6 ± 5.0	177.1 ± 7.5	<0.0001
BMI (kg/m ² , mean ± SD)	29.6 ± 5.0	29.1 ± 4.4	0.50	23.7 ± 5.2	26.8 ± 4.4	<0.0001
Waist circumference (cm, mean ± SD)	91.2 ± 11.9	100.5 ± 11.3	<0.0001	77.7 ± 12.5	92.5 ± 12.0	<0.0001
Waist-to-hip ratio (mean ± SD)	0.84 ± 0.07	0.97 ± 0.06	<0.0001	0.78 ± 0.07	0.91 ± 0.06	<0.0001
SBP (mmHg, mean ± SD)	139.5 ± 20.4	145.1 ± 20.0	0.09	119.4 ± 16.4	131.0 ± 12.3	<0.0001
DBP (mmHg, mean ± SD)	85.1 ± 12.7	87.4 ± 11.4	0.25	76.1 ± 13.4	78.7 ± 10.4	0.16
Mean pressure (mmHg, mean ± SD)	103.2 ± 14.2	106.6 ± 13.4	0.13	90.5 ± 13.9	96.1 ± 10.0	0.003
Pulse pressure (mmHg, mean ± SD)	54.4 ± 13.9	57.7 ± 13.3	0.13	43.3 ± 8.3	52.3 ± 11.0	<0.0001
Heart rate (beats/min, mean ± SD)	64.5 ± 8.9	62.7 ± 10.1	0.25	66.3 ± 9.5	66.0 ± 10.5	0.87
Questionnaire data						
Current smoking [n (%)]	14 (14.4)	11 (16.7)	0.70	24 (27.3)	27 (32.5)	0.45
Drinking alcohol [n (%)]	35 (36.1)	36 (54.5)	0.02	40 (45.5)	51 (61.5)	0.04
Hypertensive [n (%)]	66 (68.0)	49 (74.2)	0.39	14 (15.9)	28 (33.7)	0.007
Treated for hypertension [n (%)]	47 (48.5)	35 (53.0)	0.57	4 (4.5)	6 (7.2)	0.46
Biochemical data						
Total cholesterol (mmol/l, mean ± SD)	5.73 ± 1.01	5.36 ± 1.08	0.03	4.85 ± 0.97	5.18 ± 1.38	0.08
Serum creatinine (μmol/l, mean ± SD)	70.9 ± 13.5	91.2 ± 22.7	<0.0001	66.2 ± 12.4	85.3 ± 12.0	<0.0001

TABLE 2. Echocardiographic measurements by generation and sex

Characteristic	Parents		P	Offspring		P
	Women (n = 97)	Men (n = 66)		Women (n = 88)	Men (n = 83)	
Conventional echocardiography						
LV internal diameter (cm, mean $\pm$ SD)	4.91 $\pm$ 0.37	5.31 $\pm$ 0.43	<0.0001	4.79 $\pm$ 0.34	5.23 $\pm$ 0.34	<0.0001
Interventricular septum (cm, mean $\pm$ SD)	1.00 $\pm$ 0.17	1.10 $\pm$ 0.16	0.0003	0.81 $\pm$ 0.10	0.96 $\pm$ 0.12	<0.0001
Posterior wall (cm, mean $\pm$ SD)	0.90 $\pm$ 0.12	1.00 $\pm$ 0.13	<0.0001	0.76 $\pm$ 0.09	0.90 $\pm$ 0.09	<0.0001
Relative wall thickness (mean $\pm$ SD)	0.39 $\pm$ 0.06	0.40 $\pm$ 0.06	0.55	0.33 $\pm$ 0.03	0.36 $\pm$ 0.04	<0.0001
LV mass index (g/m ² , mean $\pm$ SD)	93.3 $\pm$ 19.6	108.3 $\pm$ 22.1	<0.0001	72.7 $\pm$ 12.8	89.7 $\pm$ 15.3	<0.0001
Ejection fraction (% , mean $\pm$ SD)	67.2 $\pm$ 7.0	63.4 $\pm$ 6.2	0.0007	62.6 $\pm$ 5.3	62.0 $\pm$ 6.4	0.52
TDI longitudinal						
Strain (% , mean $\pm$ SD)	21.0 $\pm$ 3.6	20.0 $\pm$ 4.2	0.10	22.0 $\pm$ 3.1	20.2 $\pm$ 2.9	0.0001
Strain rate (s ⁻¹ , mean $\pm$ SD)	1.27 $\pm$ 0.28	1.28 $\pm$ 0.30	0.84	1.33 $\pm$ 0.26	1.29 $\pm$ 0.30	0.41
Systolic velocity (cm/s, mean $\pm$ SD)	4.31 $\pm$ 1.1	5.06 $\pm$ 1.5	0.0003	5.40 $\pm$ 1.3	6.34 $\pm$ 1.6	<0.0001
TDI radial ^a						
Strain (% , mean $\pm$ SD)	49.7 $\pm$ 11.3	46.1 $\pm$ 9.9	0.05	54.8 $\pm$ 10.9	52.1 $\pm$ 10.2	0.21
Strain rate (s ⁻¹ , mean $\pm$ SD)	3.13 $\pm$ 1.1	3.17 $\pm$ 0.99	0.82	3.66 $\pm$ 1.1	3.56 $\pm$ 0.96	0.63
Systolic velocity (cm/s, mean $\pm$ SD)	3.40 $\pm$ 1.1	3.69 $\pm$ 1.0	0.13	3.78 $\pm$ 0.95	4.23 $\pm$ 0.90	0.004

TDI, tissue Doppler imaging.

^aNumbers of women and men are 82 and 56 in the parent generation, and 83 and 83 in the offspring generation, respectively.

Velocity averaged 5.25 cm/s (2.94–8.04 cm/s) longitudinal and 3.79 cm/s (2.18–5.54 cm/s) radial.

Table 2 lists the mean values of longitudinal and radial strain and velocities by generation and sex. Among parents, women and men had similar longitudinal strain and strain rate, whereas in the offspring generation, women had significantly greater longitudinal strain than men ($P < 0.0001$). In both generations, the radial strain ($P = 0.04$), but not strain rate ($P = 0.95$) was higher in women than in men. Overall, women had lower longitudinal and radial velocities than men (Table 2).

Covariables of strain, strain rate, and velocities

Table 3 shows the independent correlates of the longitudinal and radial strain, strain rate, and velocities, as well as ejection fraction as selected by stepwise regression in all subjects. Longitudinal strain significantly decreased with the WHR, and radial strain and strain rate with age and body weight ($P \leq 0.02$ for all; Table 3). Longitudinal and radial systolic velocities significantly and independently decreased with age ($P < 0.0001$) and female sex ($P = 0.002$). While adjusting for covariables, longitudinal and radial strain rate and velocities significantly increased with heart rate ($P \leq 0.009$). In

TABLE 3. Correlates of longitudinal and radial strain, strain rate, velocities, and ejection fraction selected by stepwise regression

Parameter	Longitudinal			Radial			EF (%)
	Strain (%)	Strain rate (s ⁻¹)	Velocity (cm/s)	Strain (%)	Strain rate (s ⁻¹)	Velocity (cm/s)	
Regression statistic							
Model R ²	0.11	0.05	0.29	0.13	0.12	0.19	0.10
Age (+10 years)							
$\beta \pm SE$	–	–	–0.30 $\pm$ 0.06	–1.66 $\pm$ 0.41	–0.12 $\pm$ 0.04	–0.15 $\pm$ 0.04	1.10 $\pm$ 0.23
			$P < 0.0001$	$P < 0.0001$	$P = 0.002$	$P < 0.0001$	$P < 0.0001$
Partial r ² (%)			17.7	7.7	4.9	6.5	6.9
Female (0,1)							
$\beta \pm SE$	–	–	–1.37 $\pm$ 0.21	–	–	–0.34 $\pm$ 0.11	2.19 $\pm$ 0.71
			$P < 0.0001$			$P = 0.002$	$P = 0.002$
Partial r ² (%)			7.6			1.9	2.6
Body weight (+1 kg)							
$\beta \pm SE$	–	–	–	–0.15 $\pm$ 0.04	–0.007 $\pm$ 0.003	–	–
				$P < 0.0001$	$P = 0.02$		
Partial r ² (%)				4.8	1.9		
WHR (+0.1)							
$\beta \pm SE$	–0.99 $\pm$ 0.20	–	–0.40 $\pm$ 0.12	–	–	–	–
	$P < 0.0001$		$P = 0.001$				
Partial r ² (%)			6.6				
Heart rate (+10 beats/min)							
$\beta \pm SE$	–	0.04 $\pm$ 0.016	0.22 $\pm$ 0.08	–	0.16 $\pm$ 0.06	0.23 $\pm$ 0.05	–
		$P = 0.005$	$P = 0.009$		$P = 0.005$	$P < 0.0001$	
Partial r ² (%)		2.3	1.8		1.5	4.6	

We performed stepwise multiple regression to assess the independent correlations of strain and strain rate with sex, age, anthropometric characteristics [height, weight, BMI, waist circumference, and waist-to-hip ratio (WHR)] and heart rate. β indicates the partial regression coefficients. EF, ejection fraction. Variance inflation factors (VIFs) were less than 2.00 for all explanatory variables with exception of VIF for the WHR in relation to longitudinal velocity (VIF = 2.51).

TABLE 4. Association between longitudinal systolic function and blood pressure in 334 individuals

Model	BP component	Strain (%)		Strain rate (s ⁻¹)		Velocity (cm/s)	
		Parameter estimate (95% CI)	P	Parameter estimate (95% CI)	P	Parameter estimate (95% CI)	P
Model 1	Systolic	−0.41 (−0.85 to 0.024)	0.06	−0.015 (−0.053 to 0.023)	0.43	−0.14 (−0.32 to 0.040)	0.13
Model 2	Diastolic	−0.59 (−1.02 to −0.16)	0.007	−0.025 (−0.062 to 0.013)	0.20	−0.11 (−0.28 to −0.070)	0.23
Model 3	Systolic	0.04 (−0.58 to 0.66)	0.90	0.004 (−0.049 to 0.057)	0.88	−0.12 (−0.37 to 0.13)	0.34
	Diastolic	−0.62 (−1.23 to −0.01)	0.04	−0.028 (−0.08 to 0.025)	0.30	−0.023 (−0.27 to 0.22)	0.85
Model 4	Pulse pressure	−0.02 (−0.43 to 0.39)	0.92	0.001 (−0.033 to 0.035)	0.96	−0.084 (−0.25 to 0.078)	0.31
Model 5	Mean arterial pressure	−0.55 (−0.97 to −0.12)	0.01	−0.022 (−0.059 to 0.015)	0.25	−0.13 (−0.30 to −0.047)	0.15
Model 6	Pulse pressure	0.22 (−0.21 to 0.66)	0.31	0.011 (−0.026 to 0.048)	0.56	−0.044 (−0.22 to 0.13)	0.62
	Mean arterial pressure	−0.64 (−1.10 to −0.18)	0.007	−0.027 (−0.067 to 0.014)	0.19	−0.11 (−0.30 to 0.080)	0.25

Parameter estimates [95% confidence interval (CI)] indicated changes in the left ventricular longitudinal systolic function associated with a 1 SD increase in SBP and DBP, mean arterial pressure, and pulse pressure. All parameter estimates were adjusted for family clusters, center, sex, age, body weight, heart rate, and antihypertensive drug treatment. Model 1 and model 2 included single BP component (SBP or DBP). Model 3 included both BP components (SBP and DBP). Model 4 and model 5 included single BP component (pulse pressure or mean arterial pressure). Model 6 included both pulse pressure and mean arterial pressure.

contrast, ejection fraction significantly and independently increased with age ($P < 0.0001$) and female sex ($P = 0.002$). The explained variance totaled 11.0 and 13.4% for longitudinal and radial strain, 5.0 and 11.9% for longitudinal and radial strain rate, and 29 and 19% for longitudinal and radial velocities, respectively.

Multivariable-adjusted association between left ventricular systolic tissue Doppler imaging indexes with blood pressure components

The multivariable-adjusted estimates (95% CI) associated with a 1-SD increase in SBP, DBP, MAP, or PP are shown in Table 4 for the longitudinal and in Table 5 for the radial indexes of left ventricular systolic function. All models were adjusted for family clusters, center, sex, age, body weight, heart rate, and antihypertensive drug treatment. Models 1, 2, 4, and 5 also included one of the blood pressure components (SBP, DBP, PP, or MAP). Models 3 and 6 included both SBP and DBP or both PP and MAP, respectively.

In single BP component models, longitudinal strain, but not strain rate or velocity, decreased with higher DBP ($P = 0.007$; model 2 in Table 4) and MAP ($P = 0.01$; model 5 in Table 4). The inverse association between longitudinal strain and DBP remained significant ($P = 0.04$) in model 3, which additionally included SBP. The association between longitudinal strain and MAP also remained significant ($P = 0.007$) in model 6, which further adjusted for PP (Table 4).

In multivariable-adjusted models, radial systolic strain and strain rate significantly increased with SBP ($P \leq 0.03$; model 1 in Table 5). In model 3, which included both SBP and DBP components (Table 5), both BP components were significantly correlated with radial strain and strain rate and the effects were opposite in direction. These associations were positive for SBP ($P < 0.0001$) and negative for DBP ($P \leq 0.04$). Accordingly, radial strain ($P < 0.0001$) and strain rate ($P \leq 0.0005$) were associated with higher PP even if MAP was added to the PP model (Table 5). Radial velocity was directly correlated with DBP ($P = 0.003$) and MAP ($P \leq 0.003$; Table 5).

Figure 1 shows radial strain (panel a) and strain rate (panel b) in relation to SBP at various levels of DBP in continuous analyses adjusted for the covariables. At any given level of SBP, radial strain ($P = 0.001$) and strain rate ($P = 0.04$) increased with lower DBP, again confirming that left ventricular systolic radial function was directly and independently associated with PP.

In sensitivity analysis including only 254 untreated patients, our findings remained consistent. Longitudinal systolic strain ($P = 0.01$) decreased significantly with MAP, whereas radial strain ($P = 0.0005$) and strain rate ($P = 0.03$) increased with PP (Supplemental Tables S1 and S2, <http://links.lww.com/HJH/A143>).

We also observed a direct association between radial strain and central PP in analyses including a subgroup of 206 patients from Gdansk and Cracow, in whom we

TABLE 5. Association between radial systolic function and blood pressure in 304 individuals

Model	BP component	Strain (%)		Strain rate (s ⁻¹)		Velocity (cm/s)	
		Parameter estimate (95% CI)	P	Parameter estimate (95% CI)	P	Parameter estimate (95% CI)	P
Model 1	Systolic	1.68 (0.17 to 3.19)	0.03	0.26 (0.12 to 0.39)	0.0002	0.18 (0.047 to 0.31)	0.008
Model 2	Diastolic	−0.61 (−2.14 to 0.93)	0.44	0.078 (−0.06 to 0.22)	0.27	0.21 (0.07 to 0.34)	0.003
Model 3	Systolic	4.01 (2.01 to 6.01)	0.0001	0.38 (0.20 to 0.55)	<0.0001	0.08 (−0.10 to 0.26)	0.41
	Diastolic	−3.38 (−5.41 to −1.36)	0.001	−0.18 (−0.35 to −0.002)	0.04	0.15 (−0.03 to 0.34)	0.10
Model 4	Pulse pressure	2.57 (1.27 to 3.87)	0.0001	0.25 (0.13 to 0.36)	<0.0001	0.06 (−0.06 to 0.18)	0.33
Model 5	Mean arterial pressure	0.42 (−1.10 to 1.94)	0.58	0.17 (0.034 to 0.31)	0.01	0.21 (0.07 to 0.34)	0.002
Model 6	Pulse pressure	2.87 (1.45 to 4.28)	<0.0001	0.22 (0.10 to 0.35)	0.0005	−0.02 (−0.15 to 0.11)	0.78
	Mean arterial pressure	−0.84 (−2.45 to 0.77)	0.31	0.07 (−0.07 to 0.21)	0.33	0.22 (0.07 to 0.36)	0.003

Parameter estimates [95% confidence interval (CI)] indicated changes in the left ventricular radial systolic function associated with a 1 SD increase in SBP and DBP, mean arterial pressure, and pulse pressure. All parameter estimates were adjusted for family clusters, center, sex, age, body weight, heart rate, and antihypertensive drug treatment. Model 1 and model 2 included single BP component (SBP or DBP). Model 3 included both BP components (SBP and DBP). Model 4 and model 5 included single BP component (pulse pressure or mean arterial pressure). Model 6 included both pulse pressure and mean arterial pressure.

FIGURE 1 Extrapolation from the multivariable-adjusted model of radial strain (panel a) and strain rate (panel b) in relation to the SBP at fixed levels of DBP. The numbers at the extrapolation lines indicate the fixed levels of DBP. P5, P25, P50, P75, and P95 are percentiles of the DBP distribution.

measured central hemodynamics using applanation tonometry (see Supplemental methods and Supplemental Table S3, <http://links.lww.com/HJH/A143>). The multivariable-adjusted association between left ventricular radial strain and central PP was similar compared with the association seen with peripheral PP (Supplemental Table S4, <http://links.lww.com/HJH/A143>).

DISCUSSION

The main finding of our study was that the steady and pulsatile components of BP were differently associated with the longitudinal and radial components of left ventricular systolic function. Radial left ventricular systolic function increased with the pulsatile component of BP as assessed by PP. Longitudinal left ventricular systolic function decreased with MAP and DBP. Thus, hemodynamic factors,

such as a chronic pulsatile hemodynamic loading on the left ventricular and longstanding high MAP, impact on left ventricular systolic function.

The steady component of BP, represented by MAP and the pulsatile component, represented by PP, play an important role in the pathophysiology of cardiovascular diseases [12]. MAP is determined by peripheral arterial resistance, which depends on the physical characteristics of the arterial tree and the volume of blood that the left ventricular ejects. In the absence of aortic stenosis, BP provides a clinically useful estimate of left ventricular afterload. There is a relation between left ventricular stroke volume and aortic compliance in the determination of central and peripheral PP. On one hand, if aorta is non-compliant, the greater the left ventricular stroke volume, the greater the changes in aortic systolic pressure during left ventricular ejection and, hence, the higher the aortic PP becomes. On the other hand, if the aorta is compliant, the aortic walls elastically expand to accommodate the ejected blood during systole. An elastic aorta, therefore, dampens pulsatility and maintains a continuous blood flow from the heart to the periphery. In other words, aortic PP reflects pulsatile stress and aortic rigidity [13]. Furthermore, PP is amplified with increasing distance from the aortic root especially in younger patients [14]. Thus, peripheral (brachial) PP is not always the perfect surrogate for aortic PP. Relationships between an elevated peripheral PP and left ventricular hypertrophy [15], impaired left ventricular relaxation [16], and symptomatic heart failure [17,18] have been reported previously. On the contrary, recent clinical studies [19–22] have also demonstrated that left ventricular mass, left ventricular diastolic function, and intima-media thickness were more strongly related to central pressures than to peripheral pressures. However, a recent meta-analysis provided no evidence that aortic PP is predictive of cardiovascular mortality and morbidity over and beyond pressures measured at periphery [23].

The heart is a complex three-dimensional structure consisting of myocytes laid out in different directions [24]. Longitudinal movement of the left ventricular results from contraction of longitudinally oriented subendocardial and subepicardial fibers, whereas radial left ventricular wall thickening mainly originates from contraction of circumferential fibers located in the mid-wall [24]. Gould *et al.* [25] assessed the relation between the directional components of left ventricular contraction and ejection fraction in 122 patients with or without heart disease, by using angiocardigraphy. The contribution of the longitudinal and radial components to total cardiac work was 14 and 40%, respectively [25]. In other words, the radial function builds up the pressure, whereas the longitudinal function serves more to accommodate the 'volume' load of the left ventricle. Thus, separate analysis of the various components of left ventricular systolic function might be important for understanding the progression of left ventricular systolic dysfunction at different stages of heart disease [26].

In our study, the multivariable-adjusted longitudinal strain, strain rate, and velocity significantly decreased with higher MAP. Along similar lines, some clinical studies found depressed left ventricular longitudinal function in patients with hypertension as compared with normotensive controls

[1–4,27,28]. Baltabaeva *et al.* [4] reported an inverse correlation between longitudinal basal strain and MAP in 74 untreated hypertensive patients and 34 normotensive individuals. Changes in left ventricular deformation are determined by the fiber structure and curvature of the myocardium and its interaction with local wall stress at the beginning of ejection, which decreases from the endocardium to epicardium and from the left ventricular base to the apex [29]. Thus, increased MAP might lead to increased wall stress, particularly on the longitudinally oriented and less curved subendocardial fibers. Since the subendocardium is more vulnerable to increased wall stress, ischemia, and interstitial fibrosis, longitudinal systolic dysfunction could already been seen at the early stages of progressive myocardial disease, including hypertrophy and myocardial ischemia [30].

A recent experimental study involving an aortic banding model showed disparate changes in longitudinal and radial myocardial strain in response to acute alternations to left ventricular afterload [31]. Longitudinal systolic function dramatically fell as afterload increased, whereas left ventricular fractional shortening and radial strain were still preserved after a mild banding [31]. Along similar lines, previous studies in patients with hypertension or diabetes showed that the decreased longitudinal function appears to be compensated by increased radial function [1–4,32]. The precise mechanism of the radial compensation in these patients remains unclear. One possible explanation might be linked to left ventricular wall stress. Because of differences in the left ventricular curvature, left ventricular wall stress is usually lower circumferentially than longitudinally [29]. Thus, at higher pressures, longitudinal wall stress is increased, which impairs deformation of the myofibers in this direction. To maintain stroke volume under these conditions, circumferential fibers take over part of the cardiac work. In line with this mechanism, left ventricular radial systolic function increased with higher systolic pressure. In addition, the multivariable-adjusted model showed that at any given level of SBP, radial strain and strain rate also increased with lower DBP. Thus, chronic increase in PP increases left ventricular load and enhances left ventricular radial systolic performance, and might in long run lead to left ventricular hypertrophy and increase in left ventricular oxygen requirements. This mechanism probably contributes to development and progression of left ventricular dysfunction in hypertensive patients.

In our study, we described the association of the radial and longitudinal left ventricular strain with steady and pulsatile BP components measured at the brachial artery. Whereas MAP and DBP almost do not change from the aortic root to brachial artery, PP is more dynamic and is amplified with increasing distance from the aortic root, especially in younger individuals. Thus, it might seem likely that aortic (central) PP should demonstrate a more significant association with left ventricular function than brachial (peripheral) PP. To address this issue, we also analyzed the association between left ventricular radial strain and central PP in a subgroup of 206 individuals. We found that the association of left ventricular radial strain with central PP was similar to the association with peripheral (brachial) PP (as the effect sizes were 2.26 vs. 2.57%, respectively).

The present study must be interpreted within the context of its potential limitations and strengths. First, strain and strain rate TDI imaging is prone to measurement error due to signal noise, acoustic artifacts, and angle dependency. This may limit the application of TDI in routine clinical practice. Newer techniques, such as ‘speckle tracking’ algorithms, might be less vulnerable to these artifacts [33]. However, TDI offers superior temporal resolution, which is important particularly in assessing the radial component of left ventricular systolic function, in comparisons with speckle tracking or MRI techniques. Second, although we optimized the angle of the ultrasound beam, the velocity range settings and noise level, we could not always acquire images of optimal quality, especially for assessment of radial strain and strain rate. Thus, we had to discard 52 individuals from the analysis of radial strain. Left ventricular axis deviation (older individuals) and a thinner myocardial wall (younger individuals) often lead to nonperpendicular alignment of the ultrasound beam or artifacts due to endocardial and epicardial reflections, respectively. These factors reduce the accuracy of the TDI technique in the assessment of the radial strain. Third, we estimated longitudinal strain and strain rate only from the basal segment of the inferior and inferolateral left ventricular free walls. We might therefore have underestimated the full spectrum of longitudinal or radial deformation along and between the left ventricular walls. However, the objective of our study was to explore the effects of different BP components on radial and longitudinal left ventricular strain measured at the same segment of the left ventricular wall and, therefore, clarify the possible mechanism that might contribute to development and progression of left ventricular dysfunction associated with higher PP. Finally, BP was measured in the seated position, whereas echocardiography for left ventricular systolic function was recorded at the same day but at a different time point in the partial left lateral decubitus position. However, the results on association between left ventricular radial strain and sitting brachial BPs were similar compared with the associations seen with supine central pressures or supine brachial BPs in a subgroup of 206 individuals in whom both supine and sitting BP measurements were available (Supplemental Table S4, <http://links.lww.com/HJH/A143>).

In conclusion, our study is the first to describe in a general population the association of radial and longitudinal left ventricular strain with various BP components analyzed on a continuous scale. We demonstrated that left ventricular radial function increased with PP, the pulsatile BP component, whereas longitudinal function decreased with the steady component of BP as expressed by MAP or DBP. It sets the agenda for clinical practice and research. From the clinical point of view, our study underscores the importance of BP, particularly PP, as the mediator of left ventricular systolic dysfunction. In an era in which isolated systolic hypertension affects about 30% of the elderly (60 years), controlling BP to target levels is of paramount importance to block the transition from left ventricular dysfunction to overt heart failure. From the research point of view, further studies should clarify the mechanism underlying the increase in left ventricular radial strain in response to SBP and PP and the decrease in longitudinal

strain in response to MAP. Clarifying these mechanisms might open new opportunities for prevention and treatment of early left ventricular dysfunction.

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Conflicts of interest

There are no conflicts of interest.

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