The International Journal of Cardiovascular Imaging (2019) 35:327–337
https://doi.org/10.1007/s10554-018-1474-2

ORIGINAL PAPER

Post-systolic shortening: normal values and association with validated echocardiographic and invasive measures of cardiac function

Philip Brainin[1] · Sofie Reumert Biering-Sørensen[1] · Rasmus Møgelvang[1] · Martina Chantal de Knegt[1] · Flemming Javier Olsen[1] · Søren Galatius[1] · Gunnar Hilmar Gislason[1] · Jan Skov Jensen[1] · Tor Biering-Sørensen[1]

Received: 14 August 2018 / Accepted: 12 October 2018 / Published online: 19 October 2018

Abstract

Post-systolic shortening (PSS) does not contribute to the ejection of blood and may inhibit diastolic filling. We determined normal values of PSS in healthy subjects and investigated associations with echocardiographic and invasive measures of systolic and diastolic function. We prospectively analyzed participants from the general population (n = 620, mean age 47 ± 14 years) with no cardiovascular disease. Participants underwent echocardiography, including speckle tracking assessment of the post-systolic index (PSI), strain and time. We defined the PSI as: 100 × [(peak global longitudinal strain − peak systolic longitudinal strain)/(peak global longitudinal strain)]. We also included stable patients (n = 44) referred for left ventricle (LV) catheterization and echocardiography. Normal values: median PSI 2.0% (IQR 0.7, 4.8), post-systolic strain 0.4% (IQR 0.2, 0.8) and post-systolic time 22.6 ms (IQR 10.7, 40.8). Sex modified the relationship between PSI and age (P interaction = 0.037), such that PSI increased with age in women but not in men. PSI was associated with diastolic function (e′, E/e′ and E/A) (P < 0.05 for all), but not with LV ejection fraction (P = 0.08). PSI was associated with invasively measured LV pressure decline in early diastole, dP/dt min ($\beta = 0.12$, P = 0.010), but not with LV pressure rise in early systole, dP/dt max ($\beta = -0.05$, P = 0.30). A PSI > 5% had 82% specificity and 99% sensitivity for identifying impaired LV systolic and/or diastolic function. Normal values of PSS are modified by sex. The PSI is associated with most validated echocardiographic and invasive measures of cardiac systolic and diastolic function.

Keywords Deformation · Delayed · Shortening · Echocardiography · Hibernation

Introduction

In recent years, new imaging techniques of the heart have allowed for detailed, non-invasive assessments of the cardiac cycle [1]. Using speckle tracking echocardiography (STE), quantitative evaluation of even subtle changes in cardiac deformation has become possible. Consequently, new and promising markers for diagnosis and prognosis of heart disease have been introduced, including global longitudinal strain (LS) and strain rate [2]. With the introduction of STE, new attention has been brought upon already known aspects of the cardiac cycle, including post-systolic shortening (PSS). This phenomenon represents a delayed myocardial contraction occurring after end-systole, thus not contributing to the ejection of blood [3] (Fig. 1a, b). The existence of PSS has been known for many years and it has been linked to different cardiac pathologies [4–7].

The relevancy of PSS in myocardial disease has been questioned because it also occurs in healthy individuals. Voigt et al. [8] found that PSS predominantly occurred in ischemic segments of the myocardium but also found that 30% of healthy controls exhibited some degree of PSS. Despite this ambiguous natural history, the significance of PSS has recently resurfaced as it was demonstrated as a significant predictor of cardiovascular events in a low risk general population and in patients who had recently suffered from ST-segment elevation myocardial infarction [9, 10]. Importantly, PSS may be assessed on a segmental and regional level [9, 11, 12], however, several studies have

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10554-018-1474-2) contains supplementary material, which is available to authorized users.

✉ Philip Brainin
denlillefilur@hotmail.com

[1] Department of Cardiology, Herlev and Gentofte University Hospital, University of Copenhagen, Niels Andersens Vej 65, Post 835, 2900 Hellerup, Denmark

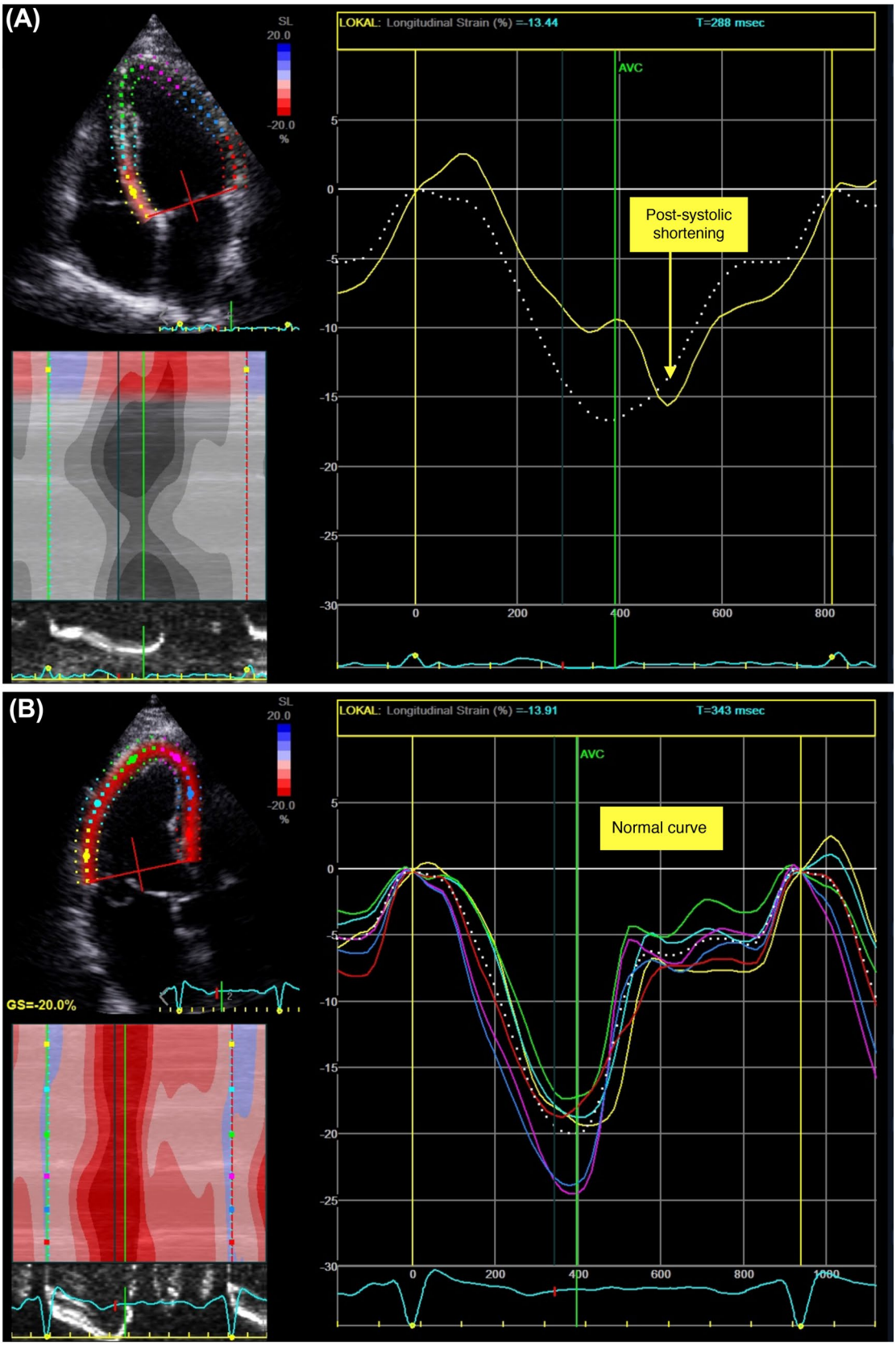

Fig. 1 Screen caption of longitudinal strain profile. **a** Yellow segment displays post-systolic shortening as indicated by yellow arrow. **b** Normal strain profile

analyzed PSS as a global phenomenon [8, 10, 13–15]. In these studies, average values of measures of PSS were summarized and derived from all myocardial segments. To fully understand the extent of PSS in healthy individuals and to delineate differences from pathological PSS, clear definitions of normal values of PSS, acquired from a large study sample, are necessary.

The objective of this study was therefore to establish normal values of measures of PSS, assessed as a global phenomenon where values were derived from all myocardial segments, and to investigate the association between measures of PSS and validated measurements of systolic and diastolic function assessed by echocardiography and left heart catheterization.

Methods

Study population

We included a subgroup of participants free of cardiovascular disease from the Copenhagen City Heart Study (study cohort I). Additionally, we included patients suspected of ischemic heart disease who underwent left heart catheterization (study cohort II). Subjects from study cohort I and II were prospectively enrolled and gave written informed consent before examination. The study conformed to the 2nd Declaration of Helsinki and was approved by the Steering Committee of the Copenhagen City Heart Study, the Danish Data Protection Agency and the local Scientific and Ethics Committee.

Study cohort I

Patients who underwent detailed echocardiographic examination, including speckle tracking analysis, included in the 4th Copenhagen City Heart Study from January 2001 to December 2003 (n = 1296). All participants were examined independently of current health conditions and risk factors. The study population has previously been described in detail [16]. We excluded participants treated with heart medication (n = 261), hypertension (n = 329), right or left bundle branch block (n = 11), diastolic dysfunction (n = 64) or ischemic heart disease (n = 11). No patients had heart failure (HF) or atrial fibrillation. After exclusion, data on measures of PSS by STE were available in 620 participants.

Study cohort II

Patients admitted from April 2009 to February 2011 with suspected stable ischemic heart disease, undergoing coronary angiography, left heart catheterization and echocardiographic examination at Department of Cardiology, Herlev and Gentofte University Hospital, Denmark. The study population has previously been described [17]. Data on PSS were available for 44 patients.

Echocardiography

Echocardiograms were performed using a 2.5-MHz transducer with a Vivid 5 ultrasound system (GE Healthcare, Horten, Norway). All participants were examined by conventional 2-dimensional echocardiography and tissue Doppler imaging (TDI). Data was stored offline and analyzed using echocardiographic software [Cohort I: Echopac version 2008, GE Medical, Horten, Norway, cohort II: Echopac version 2011 (BT12)]. Echocardiograms were carried out by experienced physicians or sonographers.

Conventional echocardiography

In study cohort I, regional function measures were carried out in accordance with the 16 standard segments model, as recommended in guidelines by the American Society of Echocardiography [18]. Evaluation of left ventricle ejection fraction (LVEF) was performed by only 1 investigator based on the wall motion score index. In study cohort II, LVEF was calculated using biplane Simpson's method. Left ventricle (LV) mass index was calculated by dividing LV mass with estimated body surface area. In the apical view, pulsed wave Doppler was applied to track inflow between the tips of the mitral valves. Peak velocity of atrial (A) and early (E) diastolic filling were measured along with E-wave deceleration time (DT). The peak longitudinal early diastolic myocardial velocity (e′) was measured with the range gate placed at the septal and lateral annular segments in the 4-chamber view and reported as the absolute value. The average value was calculated and E/e′ ratio was obtained. Left atrial volume index (LAVI) was calculated by determining the left atrial volume using the biplane area length method and then dividing this with the body surface area. Diastolic dysfunction was defined according to contemporary guidelines, where two or more of the following criteria had to be met: average $E/e' > 14$, average $e' < 9$ cm/s and LAVI > 34 mL/m^2 [19]. No information was available on tricuspid regurgitation velocity.

Speckle tracking echocardiography

Two-dimensional STE measures were obtained in the apical 4-, 3- and 2-chamber views. In study cohort I, images had an average of 57 frames/s (SD: 4 frames/s), while in study cohort II the average was 79 frames/s (SD: 18 frames/s). According to current guidelines we examined six myocardial walls in the LV, consisting of 18 myocardial segment [20]. An automated function defined a region of interest (ROI)

at end-systole. Correct tracking of speckles was secured by the responsible investigator, who visually assessed the automatically defined ROI. The ROI was correctly placed when it spanned from the endocardium to the myo-epicardial border and it followed the motion of speckles. When necessary the ROI was manually readjusted. In study cohort I, the apical 4-chamber view was available in 548 patients, 3-chamber view in 307 patients and the 2-chamber view in 410 patients. In study cohort II, the apical 4-chamber view was available in 43 patients and the 3- and 2-chamber views in all 44 patients. All strain measurements were obtained from one cardiac cycle and averaged over 18 segments. GLS was obtained by averaging the values of peak global longitudinal strain. Post-systolic strain was calculated as the absolute difference between peak global LS and peak systolic LS (Fig. 2). Post-systolic time was assessed as the difference between time at maximum strain in the cardiac cycle and time at aortic valve closure (AVC). Timing of AVC was assessed by tissue Doppler M-mode. We defined the post-systolic index (PSI) as: $100 \times [(\text{peak global LS} - \text{peak systolic LS})/(\text{peak global LS})]$. If the maximum longitudinal shortening was within the systole, PSI was set to zero. PSI was summarized and averaged to provide a mean value. As described in a previous study, we found low intra- and inter-observer variability with only small bias for calculations of PSI in study cohort I (mean difference ± 1.96 SD for intraobserver 0.25 ± 0.74 and 0.06 ± 0.56 for interobserver analysis) [10].

Invasive measures

In study cohort II, all patients underwent left heart catheterization to determine LV pressures [21]. Firstly, a 5 French fluid filled pigtail catheter was placed in the LV chamber and secondly, the pressure was set and transducer calibrated. Thereafter, invasively measured pressure curves were obtained over the course of minimum 3 cardiac cycles. LV pressure curves were saved offline and digitalized (Dagra Version 2.0.12.35924). The LV catheterization provided information on the rate of LV pressure rise in early systole (dP/dt max), rate of LV pressure decline in early diastole (dP/dt min), the time constant of LV isovolumic pressure decline (tau) and peak systolic pressure. All measures were averaged over the number of cardiac cycles. Multivessel disease was defined as a coronary artery stenosis ≥ 50% in two or more of the following coronary vessels: left anterior

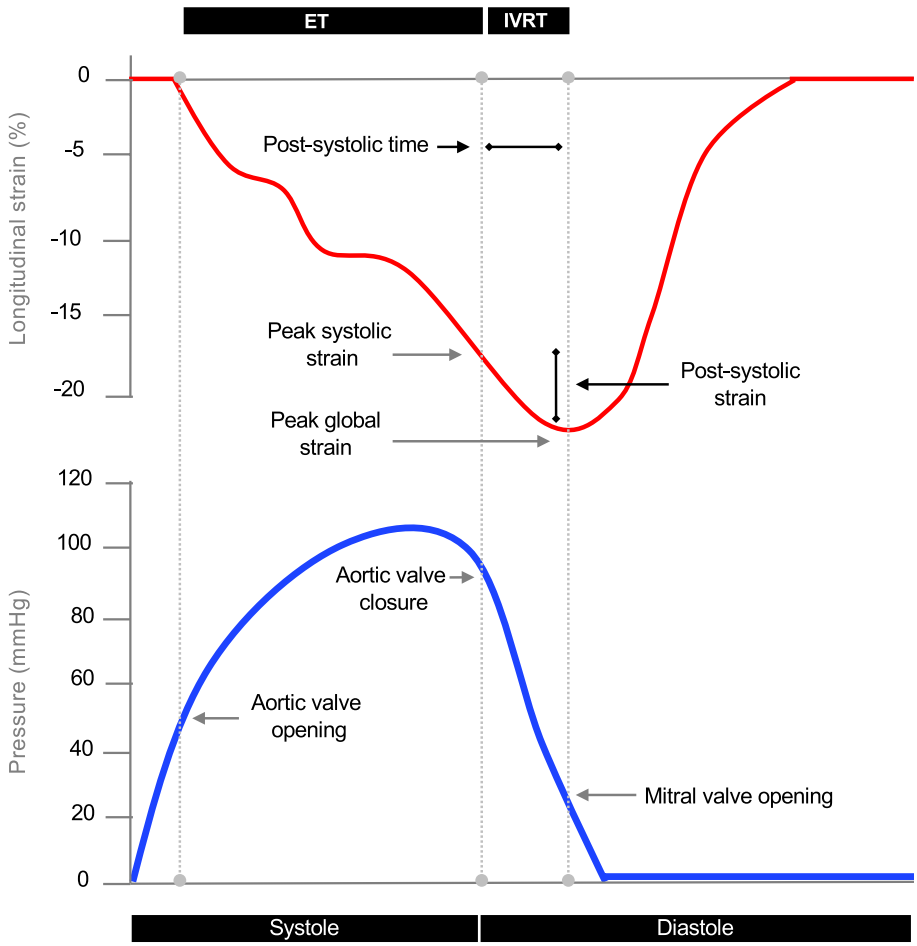

Fig. 2 Schematic drawing of longitudinal strain profile and pressure changes in the left ventricle during the cardiac cycle. Red line represents longitudinal strain (%). Blue line represents pressure (mmHg). *ET* ejection time, *IVRT* isovolumetric relaxation time

descending artery, right coronary artery and left circumflex artery.

Statistics

Proportions were compared using X^2 test, Students *t* test for continuous Gaussian distributed variables and Wilcoxon rank-sum for non-Gaussian distributed variables. P for trend was calculated using linear regression models and Chi square test for trend. All PSS measurements, comprising PSI, post-systolic strain and time, showed non-Gaussian distributions that were transformed using a natural logarithmic model. Associations between PSS measurements and echocardiographic and invasive measurements were tested using univariable regression analyses. Age category difference was assessed by oneway ANOVA test using log-transformed values of the PSI, post-systolic strain and post-systolic time. Restricted cubic spline models were constructed to assess the association between age and measurements of PSS. We regarded P-values ≤ 0.05 in 2-sided tests as statistically significant. All analyses were performed using Stata SE version 13.1 (StataCorp LP, College Station, TX).

Results

Normal values by age and sex

Study cohort I consisted of 620 participants (female 56%) with mean age 47 ± 14 years (Table 1). In healthy subjects the prevalence of PSS, defined as PSI > 0%, was 80% and normal values of measures of PSS were: median PSI 2.0% (IQR 0.7, 4.8), median post-systolic strain 0.4% (IQR 0.2, 0.8) and median post-systolic time 22.6 ms (IQR 10.7, 40.8). We stratified subjects according to sex and a priori defined age categories: 20–39, 40–59 and ≥ 60 years (Table 2). Sex modified the relationship between PSI and age (P interaction = 0.037), such that PSI increased significantly across categories of age in women (P = 0.013) but not in men (P = 0.42) (Fig. 3a). Post-systolic strain

Table 1 Baseline clinical characteristics for study cohort I stratified by sex and study cohort II

	Study cohort I		*P* value*	Study cohort II
	Women (n = 345)	Men (n = 275)		All (n = 44)
Clinical data				
Age, years	47 ± 14	48 ± 14	0.64	65 ± 12
Systolic blood pressure (mmHg)	116 ± 12	123 ± 11	< 0.001	144 ± 27
Body mass index (kg/m^2)	23 ± 3	25 ± 3	< 0.001	27 ± 4
eGFR (mL/min per 1.73 m^2)	77 ± 13	86 ± 15	< 0.001	N/A
Heart rate (bpm)	65 ± 10	64 ± 10	0.23	69 ± 13
Diastolic dysfunction, n (%)	N/A	N/A	N/A	12 (28%)
Multivessel disease by coronary angiography, n (%)	N/A	N/A	N/A	17 (39%)
Echocardiography				
Left ventricular ejection fraction (%)	60 ± 1	60 ± 1	0.39	53 ± 8
Peak global longitudinal strain (%)	− 20.9 ± 3.2	− 20.5 ± 3.2	0.080	− 16.2 ± 3.5
Peak systolic longitudinal strain (%)	− 20.2 ± 3.6	− 20.0 ± 3.3	0.33	− 16.1 ± 4.3
Left ventricular mass index (g/m^2)	73 ± 14	88 ± 16	< 0.001	88 ± 21
E/A-ratio	1.4 ± 0.5	1.3 ± 0.5	0.16	1.0 ± 0.3
E/e′	8.6 ± 2.0	8.6 ± 1.8	0.95	10.3 ± 4.8
e′ (cm/s)	9.4 ± 2.3	8.8 ± 2.2	< 0.001	7.4 ± 2.3
Left atrial volume index, mL/m^2	18.2 ± 4.5	18.3 ± 4.9	0.78	22.2 ± 9.6
Post-systolic measures				
Post-systolic index (%)	2.0 (0.8, 4.6)	2.0 (0.7, 4.9)	0.66	7.3 (3.4, 14.3)
Post-systolic strain (%)	0.4 (0.1, 0.7)	0.4 (0.2, 0.8)	0.71	1.7 (0.7, 2.6)
Post-systolic time (ms)	24.1 (11.9, 42.0)	21.4 (8.6, 39.6)	0.14	54.3 (34.4, 82.3)

e′ average peak early diastolic longitudinal mitral annular velocity, *E*/*e′* ratio between peak transmitral early diastolic inflow velocity and average peak early diastolic longitudinal mitral annular velocity, *E*/*A* ratio between peak transmitral early and late diastolic inflow velocity, *eGFR* estimated glomerular filtration rate

*P-value for difference between women and men in study cohort I

Table 2 Normal values of post-systolic shortening according to age categories and sex in healthy participants from study cohort I (n = 684)

	Men					Women					*P* for sex diff.
	Age 20–39 (n = 71)	Age 40–59 (n = 144)	Age ≥ 60 (n = 60)	*P* for age diff.	*P* for trend	Age 20–39 (n = 99)	Age 40–59 (n = 179)	Age ≥ 60 (n = 67)	*P* for age diff.	*P* for trend	
Post-systolic measures											
Post-systolic index (%)	1.7 (0.7, 4.7)	2.2 (0.7, 4.7)	2.0 (0.5, 5.3)	0.93	0.42	1.6 (0.8, 4.2)	2.0 (0.7, 4.5)	2.5 (0.8, 5.9)	0.010	0.013	0.50
Post-systolic strain (%)	0.4 (0.2, 0.7)	0.3 (0.1, 0.8)	0.4 (0.2, 0.8)	0.60	0.35	0.3 (0.2, 0.7)	0.3 (0.1, 0.8)	0.5 (0.2, 0.9)	0.080	0.033	0.51
Post-systolic time (ms)	21.6 (6.8, 29.9)	21.1 (10.3, 39.8)	21.0 (9.0, 40.1)	0.51	0.56	24.2 (11.9, 38.4)	22.1 (10.0, 39.8)	25.1 (10.9, 55.9)	0.34	0.66	0.027

Age category difference was determined by ANOVA oneway test on natural log-transformed values of the post-systolic index, strain and time

increased by age categories in women (P = 0.033) but not in men (P = 0.35; P interaction = 0.34; Fig. 3b). Although post-systolic time was significantly higher in women as compared to men (P sex difference = 0.027), it did not increase significantly across age categories in neither women (P = 0.66) nor men (P = 0.56; Fig. 3c).

Association with echocardiographic measurements of cardiac function

Associations between PSS and markers of cardiac function by echocardiography were evaluated in study cohort I (Table 3). Increasing values of PSI, post-systolic strain and time were significantly associated with systolic function, as highlighted by a significant decrease in peak global LS (P < 0.05 for all) and peak systolic LS (P < 0.001 for all) (Supplemental Figs. 1 and 2). Interestingly, increasing PSI was associated with a higher decrease in peak systolic LS (standardized $\beta = 0.368$, $R^2 = 0.13$, P < 0.001) as compared to peak global LS (standardized $\beta = 0.223$, $R^2 = 0.05$, P < 0.001). Furthermore, increasing values of both PSI and post-systolic strain were strongly associated with significantly reduced diastolic function, determined by E/A-ratio, E/e′ and e′ (P < 0.05 for all). Post-systolic time was not associated with any of the markers of diastolic function except for e′ (P = 0.018).

Association with invasive measurements of cardiac function

Baseline clinical characteristics for study cohort II are displayed in Table 1. We found no association between PSI and the invasive measure of contractility measured by rate of LV pressure rise in early systole, dP/dt max (standardized $\beta = -0.164$, $R^2 = 0.03$, P = 0.30) (Fig. 4a). In contrast, increasing values of PSI were strongly associated with invasively assessed diastolic function defined as rate of LV pressure decline in early diastole, dP/dt min (standardized $\beta = 0.400$, $R^2 = 0.16$, P = 0.010) (Fig. 4b). No invasive measures of cardiac function were related with post-systolic strain or time. No measurements were associated with tau, peak systolic pressure or end diastolic pressure (Table 3). A sensitivity analysis showed that E/e′, E/A, e′ and LAVI were not associated with dP/dt min (P > 0.10 for all).

Diagnostic accuracy

To investigate the diagnostic accuracy for systolic and/or diastolic dysfunction we defined a 5% cut-off value of PSI based on data from study cohort I (Table 2) and findings from a recent prognostic study where patients with mean PSI above 2.5 ± 1.5% had increased risk of cardiac events [10]. We defined impaired systolic function as LVEF < 50%

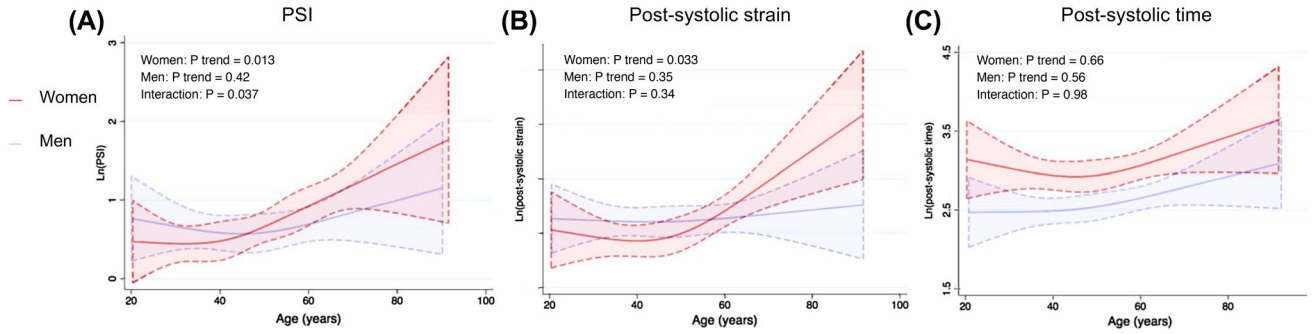

Fig. 3 Restricted cubic spline models depicting the association between age and measurements of post-systolic shortening according to sex: **a** post-systolic index (PSI), **b** post-systolic strain and **c** post-systolic time. Blue curves with 95% CI indicate men and red curves with 95% CI indicate women

Table 3 Association between post-systolic measures and echocardiographic (study cohort I) and invasive (study cohort II) measurements of cardiac systolic and diastolic function

	Post-systolic index		P-value	Post-systolic strain		P-value	Post-systolic time		P-value
	Coefficient (β)	Standardized coefficient (β)		Coefficient (β)	Standardized coefficient (β)		Coefficient (β)	Standardized coefficient (β)	
Study cohort I									
Echocardiographic measurements									
Left ventricular ejection fraction	−0.107	−0.074	0.077	−0.065	−0.049	0.240	−0.038	−0.033	0.514
Peak global LS	0.098	0.223	<0.001	0.040	0.099	0.017	0.055	0.136	0.006
Peak systolic LS	0.156	0.368	<0.001	0.094	0.257	<0.001	0.061	0.171	<0.001
E/A-ratio	−0.414	−0.151	<0.001	−0.258	−0.103	0.014	−0.168	−0.055	0.274
E/e′	0.069	0.094	0.025	0.076	0.112	0.008	0.053	0.078	0.124
e′	−0.122	−0.204	<0.001	−0.093	−0.170	<0.001	−0.069	−0.119	0.018
Left atrial volume index	0.009	0.033	0.440	0.014	0.050	0.244	0.007	0.024	0.642
Study cohort II									
Invasive measurements									
dP/dt max per 100 mmHg/s	−0.049	−0.164	0.304	−0.010	−0.032	0.845	−0.051	−0.222	0.168
dP/dt min per 100 mmHg/s	0.119	0.400	0.010	0.078	0.253	0.116	0.029	0.124	0.445
tau	0.003	0.076	0.636	0.003	0.095	0.560	−0.003	−0.101	0.535
Peak systolic pressure	−0.004	−0.114	0.479	0.001	0.033	0.838	−0.001	−0.020	0.901
End diastolic pressure	0.011	0.125	0.437	−0.002	−0.022	0.891	−0.014	−0.209	0.196

dP/dt max rate of left ventricle pressure early systole, *dP/dt min* rate of left ventricle pressure early diastole, *e′* average peak early diastolic longitudinal mitral annular velocity, *E/e′* ratio between peak transmitral early diastolic inflow velocity and average peak early diastolic longitudinal mitral annular velocity, *E/A* ratio between peak transmitral early and late diastolic inflow velocity, *LS* longitudinal strain

and diastolic dysfunction as two or more of the following: average E/e′ > 14, average e′ < 9 cm/s and LAVI > 34 mL/m^2. Using this cut-off value in study cohort II revealed the following accuracy to identify systolic and/or diastolic dysfunction: sensitivity 99%, specificity 82%, positive predictive value 84% and negative predictive value 99%.

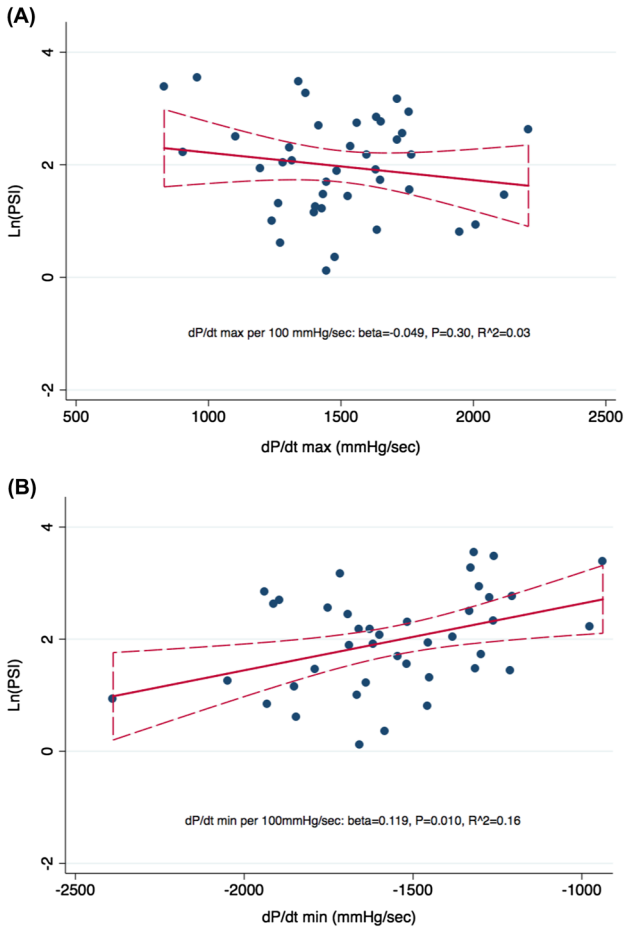

Fig. 4 Scatter plots for PSI and values of dP/dt max and dP/dt min. The center line indicates the linear association between ln (PSI) and values of **a** dP/dt max and **b** dP/dt min, respectively. The dotted red lines indicate 95% confidence intervals. dP/dt max: rate of left ventricle pressure early systole, dP/dt min: rate of left ventricle pressure early diastole

Discussion

Several studies have reported on the presence of PSS in healthy subjects [8, 10]. In healthy hearts, PSS is suggested to be a part of a well-balanced and synchronized deformation process. In myocardial disease, PSS is believed to occur due to passive elastic recoil caused by heterogeneity of myocardial segments or delayed ventricular conduction [5, 22]. For the latter reason, we excluded subjects with known left bundle branch block from the present study. Although PSS may occur in healthy hearts, the evidence to delineate physiological from pathological PSS is scarce. To address this issue, we determined normal values of measures of PSS and investigated associations between PSS and validated echocardiographic and invasive measures of systolic and diastolic function. This has not previously been reported in a population of this size.

We found that increasing PSI was associated with a steeper decline in peak systolic LS function than peak global LS, which illustrates how PSI not only is a marker of global LV function, but also relates directly to LV systolic function. Despite PSI being associated with two of the echocardiographic systolic markers, peak global and systolic LS respectively, it was not associated with LVEF. Likewise, we found no significant relationship with the invasive marker of systolic function and contractility (dP/dt max). Both LVEF and dP/dt max are often preserved in the early course of systolic dysfunction and are less sensitive compared to STE measurements. This may explain the lack of association between PSI and the invasive systolic measurements in our study.

Higher values of PSI were significantly associated with both echocardiographic and invasive (dP/dt min) markers of diastolic function. In comparison, the conventional echocardiographic markers of diastolic function (e′, E/e′, E/A and LAVI) were not significantly associated with dP/dt min. By definition, PSS occurs during the isovolumetric relaxation time (IVRT), i.e. the period which defines the earliest part of the diastole [23] and where the greatest decline in LV pressure is observed (Fig. 2). For this reason, it seems evident that PSS is closely associated with dP/dt min. Greater post-systolic contraction, as indicated by high PSI and post-systolic strain, results in decreased velocity of LV relaxation in early diastole, hence explaining the associations we found with markers of diastolic dysfunction. One study found that increased PSI, examined by STE, was a significant predictor of HF in ischemic heart disease but not of myocardial infarction [9]. This indicates that PSS potentially may play a role in diastolic dysfunction.

One previous study by Voigt et al. [8] examined the incidence and characteristics of PSS by Doppler tissue strain imaging in healthy controls of young (n = 20, age 25 ± 2 years) and old participants (n = 10, age 61 ± 8 years). They found that (i) PSI was significantly lower and (ii) post-systolic time was significantly higher in older subjects as compared to young subjects. Post-systolic strain was not significantly different between the two groups, nor did they find any interactions with sex. As opposed to these findings, we found that P trend for PSI and post-systolic strain increased across a priori defined age categories in women, and accordingly we discovered an important effect modification by sex that significantly affected the distribution of PSI in women. Previous results from the above mentioned study could have been biased by the low number of healthy controls (n = 30), thus accounting for these differences. Other studies have also confirmed the positive existence of sex differences in other echocardiographic measurements [16, 24].

Recent studies have described how age and sex interactions influence LV function, such that systolic and diastolic function often are more compromised in older women compared to men [25, 26]. In the elderly population, the

ventricular and arterial stiffness increase in both sex but has been reported to be greater in women. Consequently, elderly women display more concentric LV remodeling, which may lead to less ventricular dilatation during diastole. In the present study we found that PSI, which was associated with LV pressure decline in early diastole, increased significantly with age in women but not in men. On a hypothesis generating basis, this could be accounted for by the increased incidence of ventricular stiffness and LV remodeling which is observed with age in women and not in men [27]. Considering the role of PSS as a marker of diastolic dysfunction, this phenomenon could potentially also be associated with the increased prevalence of HF with preserved ejection fraction in women [28–30]. Another hypothesis is that hormonal changes in postmenopausal women, which have been shown to be associated with diastolic dysfunction [31–33], also may influence LV remodeling and hence occurrence of PSS. However, this should be investigated in future and larger cohorts.

In study cohort II, all measurements of PSS were increased compared to the reference values obtained from study cohort I. When applying a 5% cut-off of PSI to investigate the diagnostic accuracy of an impaired echocardiographic examination for patients in study cohort II, we found 99% sensitivity and negative predictive value. This finding strengthens the diagnostic significance and utility of measurements of PSS, but also calls for more studies to investigate if this cut-off value of PSI should differ between different populations of cardiac disease.

We demonstrated that PSS represents both systolic and diastolic function in a population of healthy individuals with no cardiovascular disease or risk factors. The PSI was superior to post-systolic strain and time with respect to cardiac function, as it was associated with most validated echocardiographic and invasive measurements. This may be due to the composite nature of PSI, which involves both peak global and peak systolic LS values, thus providing a more thorough and complete assessment of the cardiac function. Our results indicate clear differences to previous literature in terms of distribution of PSS measurements in healthy controls. With these new findings we therefore believe new considerations should be applied when regarding presence of PSS, and possibly also when PSS should be regarded as pathological. More research is needed to define when PSS in different populations accounts for diastolic and systolic function, respectively.

Strength and limitations

The study population included only participants of Caucasian descent, which limits the use of the acquired normal values to subjects of the same race. Study cohort II consisted of only 44 patients who underwent coronary angiography. Therefore, a discrepancy exists in the number of examined individuals in the two cohorts. However, we derived our normal values from study cohort I and used study cohort II to illustrate differences between healthy controls and patients with suspected cardiac disease. Importantly, because the sample size was very small in study cohort II this may have affected the statistical power when assessing post-systolic measurements in this cohort. This could potentially also explain why we found no association with the time constant of LV isovolumic pressure decline (tau). The use of STE does not allow to assess whether PSS occurs from active or passive forces, it solely measures the longitudinal deformation. We assessed LVEF using two different methods in the two study cohorts, which should be taken into consideration when evaluating associations with this parameter. This condition is increasingly prevalent in elderly and in order to include patients from all age categories we chose to keep these subjects. The frame rates for study cohort I were low for speckle tracking analyses, likely affecting the temporal resolution and potentially influencing the variability of PSS. We calculated PSS parameters as the average values obtained from all 18 LV segments, as regional strain measurements have been shown to be liable reduced inter- and intraobserver variability [20].

Conclusion

Normal values of measurements of post-systolic shortening increase with increasing age in women, but not in men. Among measurements of post-systolic shortening, the post-systolic index was significantly associated with most validated echocardiographic and invasive measures of cardiac function. The post-systolic index was mostly associated with cardiac diastolic function and may potentially act as a marker of diastolic dysfunction.

Funding Philip Brainin was supported by The Gangsted Foundation. Tor Biering-Sørensen was supported by the Fondsbørsvekselerer Henry Hansen og Hustrus Hovedlegat 2016. The sponsors had no role in the study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Compliance with ethical standards

Conflict of interest The authors report no conflicts of interest.

References

1. Edvardsen T, Bucciarelli-ducci C, Saraste A et al (2018) The year 2014 in the European Heart Journal—Cardiovascular Imaging. Part I. Eur Heart J-Cardiovasc Imaging. https://doi.org/10.1093/ehjci/jev150

2. Smiseth OA, Torp H, Opdahl A et al (2015) Myocardial strain imaging: how useful is it in clinical decision making? Eur Heart J 37:1196–1207. https://doi.org/10.1093/eurheartj/ehv529
3. Asanuma T, Nakatani S (2015) Myocardial ischaemia and postsystolic shortening. Heart. https://doi.org/10.1136/heartjnl-2013-305403
4. Weidemann F, Broscheit JA, Bijnens B et al (2006) How to distinguish between ischemic and nonischemic postsystolic thickening: a strain rate imaging study. Ultrasound Med Biol 32:53–59. https://doi.org/10.1016/j.ultrasmedbio.2005.09.003
5. Grines CL, Bashore TM, Harisios B et al (1989) Functional abnormalities in isolated left bundle branch block: the effect of interventricular asynchrony. Circulation 79:845–853
6. Bonow RO, Vitale DF, Maron BJ et al (1987) Regional left ventricular asynchrony and impaired global left ventricular filling in hypertrophic cardiomyopathy: effect of verapamil. J Am Coll Cardiol 9:1108–1116. https://doi.org/10.1016/S0735-1097(87)80315-7
7. Belohlavek M, Pislaru C, Bae R et al (2001) Real-time strain rate echocardiographic imaging: temporal and spatial analysis of postsystolic compression in acutely ischemic myocardium. J Am Soc Echocardiogr 14:360–369. https://doi.org/10.1067/mje.2001.110786
8. Voigt JU, Lindenmeier G, Exner B et al (2003) Incidence and characteristics of segmental postsystolic longitudinal shortening in normal, acutely ischemic, and scarred myocardium. J Am Soc Echocardiogr 16:415–423. https://doi.org/10.1016/S0894-7317(03)00111-1
9. Brainin P, Haahr-Pedersen S, Sengeløv M et al (2017) Presence of post-systolic shortening is an independent predictor of heart failure in patients following ST-segment elevation myocardial infarction. Int J Cardiovasc Imaging 34:751–760. https://doi.org/10.1007/s10554-017-1288-7
10. Brainin P, Biering-Sørensen SR, Møgelvang R et al (2018) Postsystolic shortening by speckle tracking echocardiography is an independent predictor of cardiovascular events and mortality in the general population. J Am Heart Assoc 7:1–11. https://doi.org/10.1161/JAHA.117.008367
11. Støylen A, Sletvold O, Skjaerpe T (2003) Post systolic shortening in nonobstructive hypertrophic cardiomyopathy with delayed emptying of the apex: a doppler flow, tissue doppler and strain rate imaging case study. Echocardiography 20:167–171. https://doi.org/10.1046/j.1540-8175.2003.03013.x
12. Terkelsen CJ, Hvitfeldt Poulsen S, Nørgaard BL et al (2007) Does postsystolic motion or shortening predict recovery of myocardial function after primary percutanous coronary intervention? J Am Soc Echocardiogr 20:505–511. https://doi.org/10.1016/j.echo.2006.10.004
13. Brainin P, Hoffmann S, Fritz-Hansen T et al (2018) Usefulness of postsystolic shortening to diagnose coronary artery disease and predict future cardiovascular events in stable angina pectoris. J Am Soc Echocardiogr 31:870–879.e3. https://doi.org/10.1016/j.echo.2018.05.007
14. Eek C, Grenne B, Brunvand H et al (2011) Postsystolic shortening is a strong predictor of recovery of systolic function in patients with non-ST-elevation myocardial infarction. Eur J Echocardiogr 12:483–489. https://doi.org/10.1093/ejechocard/jer055
15. Skulstad H, Edvardsen T, Urheim S et al (2002) Postsystolic shortening in ischemic myocardium: active contraction or passive recoil? Circulation 106:718–724. https://doi.org/10.1161/01.CIR.0000024102.55150.B6
16. Biering-Sørensen T, Biering-Sørensen SR, Olsen FJ et al (2017) Global longitudinal strain by echocardiography predicts long-term risk of cardiovascular morbidity and mortality in a low-risk general population. Circ Cardiovasc Imaging 10:e005521. https://doi.org/10.1161/CIRCIMAGING.116.005521
17. Biering-Sørensen T, Mogelvang R, Schnohr P, Jensen JS (2016) Cardiac time intervals measured by tissue Doppler imaging M-mode: association with hypertension, left ventricular geometry, and future ischemic cardiovascular diseases. J Am Heart Assoc. https://doi.org/10.1161/JAHA.115.002687
18. Lang RM, Badano LP, Mor-Avi V et al (2015) Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. https://doi.org/10.1016/j.echo.2014.10.003
19. Nagueh SF, Smiseth OA, Appleton CP et al (2016) Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American society of echocardiography and the European association of cardiovascular imaging. Eur Heart J Cardiovasc Imaging 17:1321–1360. https://doi.org/10.1093/ehjci/jew082
20. Voigt JU, Pedrizzetti G, Lysyansky P et al (2015) Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. Eur Heart J Cardiovasc Imaging 16:1–11. https://doi.org/10.1093/ehjci/jeu184
21. Biering-Sørensen T, Mogelvang R, Knegt MC, De et al (2016) Cardiac time intervals by tissue doppler imaging M-Mode: normal values and association with established echocardiographic and invasive measures of systolic and diastolic function. PLoS ONE 11:1–14. https://doi.org/10.1371/journal.pone.0153636
22. Claus P, Weidemann F, Dommke C et al (2007) Mechanisms of postsystolic thickening in ischemic myocardium: mathematical modelling and comparison with experimental ischemic substrates. Ultrasound Med Biol 33:1963–1970. https://doi.org/10.1016/j.ultrasmedbio.2007.06.003
23. Urheim S, Edvardsen T, Steine K et al (2003) Postsystolic shortening of ischemic myocardium: a mechanism of abnormal intraventricular filling. Am J Physiol Heart Circ Physiol 284:H2343–H2350. https://doi.org/10.1152/ajpheart.00320.2002
24. Biering-Sørensen T, Mogelvang R, Søgaard P, Jensen JS (2013) Prognostic value of cardiac time intervals by tissue doppler imaging m-mode in patients with acute ST-segment—elevation myocardial infarction treated with primary percutaneous coronary intervention. Circ Cardiovasc Imaging 6:457–466. https://doi.org/10.1161/CIRCIMAGING.112.000230
25. Najjar SS, Schulman SP, Gerstenblith G et al (2004) Age and gender affect ventricular-vascular coupling during aerobic exercise. J Am Coll Cardiol 44:611–617. https://doi.org/10.1016/j.jacc.2004.04.041
26. Shim CY, Park S, Choi D et al (2011) Sex differences in central hemodynamics and their relationship to left ventricular diastolic function. J Am Coll Cardiol 57:1226–1233. https://doi.org/10.1016/j.jacc.2010.09.067
27. Chen C, Sung KT, Shih SC et al (2016) Age, gender and load-related influences on left ventricular geometric remodeling, systolic mid-wall function, and NT-ProBNP in asymptomatic Asian population. PLoS ONE 11:1–15. https://doi.org/10.1371/journal.pone.0156467
28. Pandey A, Omar W, Ayers C et al (2018) Sex and race differences in lifetime risk of heart failure with preserved ejection fraction and heart failure with reduced ejection fraction. Circulation 137:1814–1823. https://doi.org/10.1161/CIRCULATIONAHA.117.031622
29. Scantlebury DC, Borlaug BA (2011) Why are women more likely than men to develop heart failure with preserved ejection fraction? Curr Opin Cardiol 26:562–568. https://doi.org/10.1097/HCO.0b013e32834b7faf
30. Dunlay SM, Roger VL, Redfield MM (2017) Epidemiology of heart failure with preserved ejection fraction. Nat Rev Cardiol 14:591–602. https://doi.org/10.1038/nrcardio.2017.65

31. Owan TE, Hodge DO, Herges RM et al (2006) Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 355:251–259. https://doi.org/10.1056/NEJMoa052256
32. Zhao Z, Wang H, Jessup JA et al (2014) Role of estrogen in diastolic dysfunction. AJP Heart Circ Physiol 306:H628–H640. https://doi.org/10.1152/ajpheart.00859.2013
33. Zhao D, Guallar E, Ouyang P et al (2018) Endogenous sex hormones and incident cardiovascular disease in post-menopausal women. J Am Coll Cardiol 71:2555–2566. https://doi.org/10.1016/j.jacc.2018.01.083