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Research Article

The septal bulge—an early echocardiographic sign in hypertensive heart disease

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Abstract

Patients in the early stage of hypertensive heart disease tend to have normal echocardiographic findings. The aim of this study was to investigate whether pathology-specific echocardiographic morphologic and functional parameters can help to detect subclinical hypertensive heart disease. One hundred ten consecutive patients without a history and medication for arterial hypertension (AH) or other cardiac diseases were enrolled. Standard echocardiography and two-dimensional speckle-tracking-imaging analysis were performed. Resting blood pressure (BP) measurement, cycle ergometer test (CET), and 24-hour ambulatory BP monitoring (ABPM) were conducted. Patients were referred to ''septal bulge (SB)'' group (basal-septal wall thickness $\geq$2 mm thicker than mid-septal wall thickness) or ''no-SB'' group. Echocardiographic SB was found in 48 (43.6%) of 110 patients. In this SB group, 38 (79.2%) patients showed AH either by CET or ABPM. In contrast, in the no-SB group (n = 62), 59 (95.2%) patients had no positive test for AH by CET or ABPM. When AH was solely defined by resting BP, SB was a reasonable predictive sign for AH (sensitivity 73%, specificity 76%). However, when AH was confirmed by CET or ABPM the echocardiographic SB strongly predicted clinical AH (sensitivity 93%, specificity 86%). In addition, regional myocardial deformation of the basal-septum in SB group was significantly lower than in no-SB group (14 $\pm$ 4% vs. 17 $\pm$ 4%; $P < .001$). In conclusion, SB is a morphologic echocardiographic sign for early hypertensive heart disease. Sophisticated BP evaluation including resting BP, ABPM, and CET should be performed in all patients with an accidental finding of a SB in echocardiography. J Am Soc Hypertens 2016;10(1):70–80.

Keywords: Septal bulge; hypertension; blood pressure monitoring; echocardiography; heart disease.

Introduction

Arterial hypertension (AH) has been well recognized as a common risk factor for cardiovascular disease.[1–5] However, a great number of early hypertensive patients never experience any symptoms,[6] and the awareness rate of AH remains low in general. Thus, early diagnosis of AH remains a challenge, particularly in a subclinical population.

It is known that left ventricular (LV) hypertrophy with different remodeling patterns is one of the major cardiac manifestations of hypertensive heart disease, and echocardiographic LV hypertrophy could be detected in 20% to 40% of patients with AH.[7–10] However, there are often no specific echocardiographic features for hypertensive patients at the early stage of disease.[11] Previous echocardiographic studies have described asymmetric septal hypertrophy with a localized septal thickening at the basal-mid

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portion in patients with hypertrophic cardiomyopathy[12,13] or aortic valve stenosis.[14,15] Basal-septal hypertrophy may also occur in a subset of older normal subjects, with normal wall thickness (WT) elsewhere, and is considered to be an age-related anatomic variant.[16,17] This morphologic echocardiographic sign is termed as septal bulge (SB), sigmoid septum, or discrete upper septal thickening or knuckle.[18] A large community-based population study reported that SB was documented frequently in elderly individuals with higher systolic blood pressure (SBP). It was shown that the overall prevalence of SB was 1.5% and was markedly higher (18%) in the eighth decades of life.[18] Although pathologic and echocardiographic observations have indicated that SB is a structural response in hypertensive patients,[19–21] the nature and significance of the SB in subclinical AH was never investigated.

In addition, despite the fact that BP can be easily measured, AH sometimes cannot be diagnosed due to the underreported BP reading in the casual or self-measured BP measurement.[22] BP measurement with appropriate tools is essential to diagnosing AH early as well as to guiding AH management. It has been shown that, besides resting BP measurement in the office, AH could be clinically diagnosed by 24-hour ambulatory BP monitoring (ABPM) as well as exercise stress test in some resting normotensive individuals.[1,23–25]

In the present study, we prospectively screened a subset of population without history and medication of AH as well as other cardiac diseases. A sophisticated clinical assessment for AH was conducted in these patients, including resting BP measurement, cycle ergometer test (CET) and ABPM. We investigated the prevalence of echocardiographic SB and its relationship with AH. We speculate that SB might represent an earlier structural adaption in response to pressure overload before LV concentric hypertrophy in AH.

Methods

This study was initiated in February 2013. The study subjects were selected from a group of 8208 consecutive patients referred to the echocardiographic laboratory in the University Hospital of Würzburg between February 2013 and February 2014. The enrollment criteria included (1) no history of AH and any heart diseases and (2) no history of medications for AH. A total of 154 eligible patients were invited to take part in the AH screen study. Forty-four patients, who refused to receive 24-hour ABPM or were unable to perform CET, were excluded. Finally, 110 patients completed this study. The screening flowchart of the study is shown in Figure 1. Standard echocardiographic examination was performed in all patients. Resting electrocardiography (ECG), resting manual BP measurement, ABPM, and CET (ECG/BP) were performed on the same day in all patients. The study was approved by Local Ethics Committee at the University of Würzburg and conducted in accordance to the Declaration of Helsinki. Written informed consent was obtained from all patients or their guardians.

Brachial BP was measured at rest. Patients were seated quietly for at least 5 minutes in a chair before the measurement. At least 2 measurements were made in each patient. Afterward, CET was performed on an electrically braked cycle ergometer (Ergometrics 900, Ergoline, Bitz, Germany) with incremental loads at 50/75/100/150 Watts (each stage for 3 minutes), until exhaustion. Brachial BP was measured every 3 minutes interval during testing. The testing was stopped when the targeted age-adjusted heart rate was achieved, or when SBP increased to more than 250 mm Hg, or when chest pain or arrhythmia occurs.

After CET, 24-hour ABPM was performed using a digital oscillometric blood pressure device (Mobil-O-Graph NG version 20, I.E.M., Germany). BP was measured every 15 minutes during the waking period (8 AM–12 PM) and every 30 minutes during the sleeping period (12 PM–8 AM). The test was considered satisfactory when at least 70% of the BP readings were valid.

AH was suggested by resting BP: SBP $\geq$ 140 mm Hg or diastolic BP (DBP) $\geq$ 90 mm Hg based on the mean of 2 or more properly measured seated BP.[1,3] Patients were defined as AH with positive CET results (SBP $\geq$ 200 mm Hg at 50, 75, or 100 Watts[26]) or positive ABPM results (mean SBP $>$ 135 mm Hg or DBP $>$ 85 mm Hg during the waking period and SBP $>$ 120 mm Hg or DBP $>$ 70 mm Hg during the sleeping period[1]) or both.

The classification of high BP was defined as: normal, SBP $<$ 120, and DBP $<$ 80 mm Hg; high-normal, SBP = 120–139 or DBP = 90–99 mm Hg; stage 1 hypertension, SBP = 140–159 or DBP = 90–99 mm Hg; stage 2 hypertension, SBP $\geq$ 160 or DBP $\geq$ 100 mm Hg.[1,3]

A standard transthoracic echocardiographic examination was performed (GE, Vingmed, Horten, Norway). Standard two-dimensional (2D) images and Doppler recordings were obtained according to guidelines.[27] All offline measurements were performed in a remote workstation (EchoPAC version 112, GE, Horten, Norway). LV end-diastolic dimension (LVEDD), end-diastolic WT of the mid septum (IVSd) and the posterior wall (LVPWd), as well as left atrial end-systolic diameter were measured in the parasternal LV long axis view. The maximum basal- and mid-septal WT was measured in the LV parasternal long-axis view. Basal-septal to mid-septal WT ratio (WT_Ratio) was calculated as the basal-septal WT divided by the mid-septal WT. Relative WT = (IVSd + LVPWd)/LVEDD was calculated. LV mass indexed for height to allometric power of 2.7 was estimated by LV cavity dimension and WT at end diastole[27]: LV mass (g) = $0.8 \times [1.04 \times (\text{LVEDD} + \text{LVPWd} + \text{IVSd})^3 - (\text{LVEDD}^3)] + 0.6$. LV ejection fraction was measured with the biplane Simpson method in the apical 4- and 2-chamber views. Mitral annular plane systolic

excursion was measured as well as tricuspid plane annular systolic excursion was obtained by M-mode in the apical 4-chamber view.

Pulsed-wave Doppler was performed in the apical 4-chamber view to obtain mitral inflow velocities for LV filling pattern evaluation. Peak velocity of early (E) and late (A) diastolic filling and deceleration time of E wave (DT) were measured as well as the E/A ratio was calculated. Tissue Doppler early diastolic mitral annular velocity (E′) was obtained at the septal annular site. If necessary isovolumetric relaxation time and pulmonary venous flow was evaluated and diastolic function was graded according to recent guidelines.[28]

The maximum basal- and mid-septal WT was measured in the LV parasternal long-axis view. SB was defined as the basal-septal WT $\geq$ 2 mm thicker than the mid-septal WT. Patients were divided into two subgroups according to the presence or absence of SB (SB group and no-SB group).

Reproducibility of basal- and mid-septal WT was studied using Bland and Altman analysis. The same recordings were used in consecutive 30 subjects (Patient ID 1–30). Repeated measurements blinded to the initial results were performed by one investigator (D.L.) to assess intraobserver variation, and by two investigators (D.L. and P.D.G.) to obtain interobserver variation.

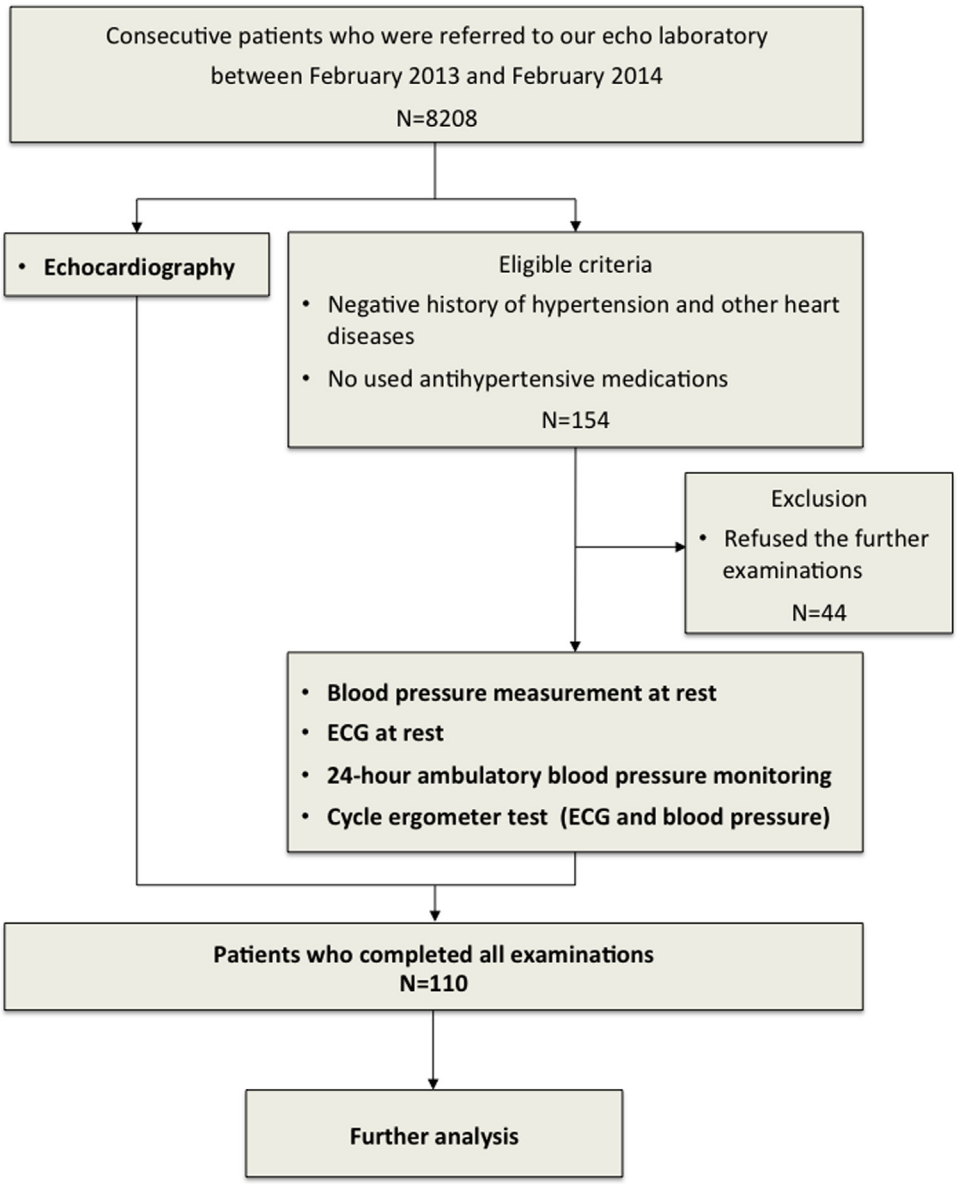

Figure 1. Screening flowchart of the study population.

Regional myocardial dysfunction was assessed by off-line speckle-tracking derived strain rate imaging with dedicated software (EchoPAC, version 112, GE, Horten, Norway). All 2D gray scale images of the standard apical 4-chamber view were recorded with a frame rate of 50 to 80 frames per second. A region of interest was created by manually outlining the endocardial border at end-systolic frame on the apical 4-chamber view. The system automatically tracked the tissue within the region and divided the myocardium into six segments. Segmental and global longitudinal strain curves were obtained and longitudinal peak systolic strain was measured in the basal, mid, and apical segments of the septal and lateral walls.

A standard 12-lead resting ECG was recorded with a paper speed of 50 mm/s and an amplification of 0.1 mV/mm. A normal axis deviation was defined as the mean electrical axis between 0° and +90°. Less than 0° was termed a left axis deviation and greater than +90° was termed a right axis deviation. The electrocardiographic voltage criterion for LV hypertrophy was defined according to Sokolow-Lyon index: $SV_1 + RV_5$ or RV_6 is greater than 3.5 mV. The ST-segment depression was defined as horizontal or down-sloping depression ≥1.0 mm at 80 ms after J-point, lower than baseline level in at least two leads.[29]

Exercise ECG was recorded continuously during CET. ECG was printed every 3 minutes interval during exercise and at least 5 minutes of recovery while the patient was sitting on the bicycle. The criteria for ischemia in ECG during exercise and recovery were any horizontal or down-sloping ST-segment depression ≥1.0 mm at 80 ms after J-point.[30]

Continuous variables were presented as mean ± standard deviation and categorical variables as percentages. Differences on continuous data between two subgroups were compared using an unpaired Student's *t* test or Mann-Whitney test. Categorical data were compared between groups using a chi square test or Fisher's exact test, as appropriate. The receiver operating characteristic analysis was performed to evaluate the predictive value of SB for indicating AH. A lineal regression of the quantitative parameter of SB (WT_Ratio) associated with the classification of AH (normal, high-normal, stage 1, and stage 2 hypertension), as well as a logistic regression analysis of WT_Ratio associated with AH were conducted, respectively. Statistical significance was defined as $P < .05$ (two-tailed test). Statistical analysis was performed using IBM SPSS, version 22 for Windows (SPSS).

Results

Among the 110 study patients, the reasons for the echocardiographic examination included as follows: routine check-up (n = 82, done in individuals who underwent check-up prechemotherapy, check-up preoperation, or in patients with high risk of heart diseases such as high-risk lipid levels or smoking), unclear thoracic pain (n = 17), dizziness or syncope (n = 6), dyspnea (n = 2), unclear palpitation (n = 1), check-up for living kidney donation (n = 1), or thoracic trauma (n = 1). The average age was 51 years (range, 22–74 years), and 54% of patients were male. Clinical and BP characteristics of patients without and with SB are shown in Table 1. SB was evidenced in 48 (43.6%) patients. Patients with SB were older and had higher body mass index as compared to patients without SB. SBP and DBP at rest and during ABPM, as well as SBP during CET were significantly higher in SB group than in no-SB group.

Resting BP was elevated in 44 (40%) patients. There were 12 (19.4%) patients with elevated resting BP in no-SB group (n = 62), whereas all of them (100%) tested negative for AH by CET and ABPM suggesting a ''white-coat'' hypertension in these12 patients. In SB group (n = 48), 32 had a resting AH and 2 of 32 (6.25%) patients with elevated resting BP showed a negative result for AH by CET and ABPM.

There were 66 (60%) patients with normal resting BP. In no-SB group, 3 of 50 (6%) patients with normal resting BP tested positive for AH by CET or ABPM. Conversely, in SB group, 8 of 16 (50%) patients with normal resting BP was diagnosed as AH by CET or ABPM. Consequently, 38 (79.2%) patients in SB group were diagnosed as AH by CET or ABPM. In contrast, in no-SB group, only 59 (95.2%) patients tested negative for AH by CET or ABPM.

During resting BP measurement, there were 15 patients with high-normal BP in SB group, AH was diagnosed in 7 patients (46.7%) by CET or ABPM. In no-SB group, high-normal BP was found in 33 patients and only 3 (9.1%) of these patients had positive test for AH by CET or ABPM.

The diagnostic performance of SB to identify AH is listed in Table 2. When AH was solely diagnosed by resting BP, SB was a reasonable predictive sign for AH (sensitivity 73%, specificity 76%). However, when AH was confirmed by CET or ABPM the echocardiographic SB strongly predicted clinical AH with a sensitivity of 93% and a specificity of 86%.

Standard echocardiographic parameters are listed in Table 3. LVEDD, LV mass indexed (mean, 63 g/m^2; range, 26–95 g/m^2), and global systolic function (LV ejection fraction, mitral annular plane systolic excursion, tricuspid annular plane systolic excursion) remained normal and were similar between no-SB group and SB group. Most patients (98.2%) had normal or slightly reduced diastolic function (= stage abnormal relaxation), and 2 (1.8%) patients had advanced diastolic dysfunction (pseudonormal filling pattern). Abnormal relaxation filling pattern was more frequently found in SB group than in no-SB group (SB group 63% vs. no-SB group 24%). No patient showed a dynamic LV outflow tract obstruction.

Table 1
Clinical and blood pressure characteristics

	Total	No-SB	SB	*P* Value
	n = 110	n = 62	n = 48	
Age, years	51 ± 13	49 ± 13	54 ± 12	.024
Male, n (%)	59 (54%)	32 (52%)	27 (56%)	.629
Height, cm	174 ± 9	173 ± 8	174 ± 10	.587
Weight, kg	77 ± 15	73 ± 14	81 ± 15	.014
BMI, kg/m^2	25 ± 4	24 ± 4	26 ± 4	.009
BSA, m^2	1.90 ± 0.21	1.87 ± 0.20	1.95 ± 0.22	.041
Resting BP (mm Hg)				
SBP	129 ± 23	120 ± 15	141 ± 27	<.001
DBP	85 ± 11	81 ± 10	90 ± 11	<.001
24-hour ABPM (mm Hg)				
Day SBP	126 ± 13	120 ± 7	132 ± 14	<.001
Day DBP	78 ± 9	76 ± 7	82 ± 10	.001
Night SBP	113 ± 12	109 ± 9	116 ± 22	.055
Night DBP	68 ± 10	65 ± 9	72 ± 11	.001
Cycle ergometer test (mm Hg)				
100 W SBP	176 ± 25	164 ± 18	190 ± 26	<.001
100 W DBP	92 ± 12	91 ± 10	95 ± 14	.085
AH defined by CET or ABPM, n (%)	41 (37.3%)	3 (4.8%)	38 (79.2%)	<.001
AH defined by resting BP, n (%)	44 (40.0%)	12 (19.4%)	32 (66.7%)	<.001
Normal	18 (16.4%)	17 (27.4%)	1 (2.1%)	
Prehypertension	48 (43.6%)	33 (53.2%)	15 (31.3%)	
Stage 1 hypertension	29 (26.4%)	9 (14.5%)	20 (41.7%)	
Stage 2 hypertension	15 (13.6%)	3 (4.8%)	12 (25.0%)	

ABPM, ambulatory blood pressure monitoring; AH, arterial hypertension; BMI, body mass index; BP, blood pressure; BSA, body surface area; CET, cycle ergometer test; DBP, diastolic BP; SB, septal bulge; SBP, systolic BP.

As expected, the mean basal-septal WT was significantly thicker in SB group (12 mm; range, 9–15 mm) than in no-SB group (8 mm; range, 5–11 mm; $P < .001$). WT_Ratio is a quantitative parameter of SB. Lineal regression analysis demonstrated a moderate correlation of the WT_Ratio with the AH classification (normal, high-normal, stage 1, and stage 2 hypertension) by resting BP: model-adjusted $R^2 = 0.461$ for age, gender, and BMI, $P < .001$. The logistic regression analysis showed a moderately strong relationship between CET or ABPM defined AH and WT_Ratio ($R^2 = 0.576$) after adjusted for age, gender, and BMI. A 0.1 point increase in the WT_Ratio was associated with 2.3-fold increase in risk of AH (odds ratio 2.32, 95% confidence interval [CI] 1.66–3.23, $P < .001$, Table 4). The receiver operating characteristic curves analysis (Figure 2A/B/C) demonstrated that the diagnostic performance of WT_Ratio for AH by CET or ABPM was significantly better than by resting BP [area under the curve 0.90 (95% CI 0.83–0.96) vs. 0.76 (95% CI 0.66–0.85), $P = .018$]. In case of Figure 2C, performance of WT_Ratio was showed in patients with normal resting BP [area under the curve 0.78 (95% CI 0.61–0.95), $P = .003$].

In addition, relative WT was significant different between no-SB group and SB group too, $P = .002$. Speckle tracking–derived longitudinal systolic strain at the basal-septal segment was significantly lower in SB group than in no-SB group (14% ± 4% vs. 17% ± 4%, $P < .001$, Table 5). Figure 3 illustrates the examples of segmental longitudinal systolic strain curves derived from speckle tracing imaging in patients with or without SB. As shown in Figure 4, longitudinal systolic strain at the basal-septal

Table 2
Predictive value of the presence of septal bulge for artery hypertension

	AH Defined by Resting BP		AH Defined by CET or ABPM	
	Estimated Value	95% CI	Estimated Value	95% CI
Sensitivity	0.73	0.57–0.85	0.93	0.79–0.98
Specificity	0.76	0.63–0.85	0.86	0.74–0.92
Positive predictive value	0.67	0.51–0.79	0.79	0.65–0.89
Negative predictive value	0.81	0.68–0.89	0.95	0.86–0.99

ABPM, ambulatory blood pressure monitoring; AH, arterial hypertension; BP, blood pressure; CET, cycle ergometer test; CI, confidence interval.

Table 3
Echocardiographic characteristics

	Total	No-SB	SB	*P* Value
	n = 110	n = 62	n = 48	
LVEDD, mm	45 ± 6	45 ± 5	45 ± 6	.956
Mid IVSd, mm	8.3 ± 1.3	7.9 ± 1.2	8.7 ± 1.3	.001
LVPWd, mm	8.2 ± 1.1	7.8 ± 1.1	8.6 ± 1.0	<.001
RWT	0.37 ± 0.07	0.35 ± 0.06	0.39 ± 0.07	.002
Basal IVSd, mm	9.8 ± 2.4	8.0 ± 1.2	12.0 ± 1.4	<.001
WT_Ratio	1.18 ± 0.23	1.02 ± 0.07	1.40 ± 0.17	<.001
LVM indexed for height$^{2.7}$ (g/m$^{2.7}$)	26.9 ± 6.7	25.6 ± 6.1	28.7 ± 7.2	.021
LAD, mm	33 ± 6	32 ± 5	34 ± 7	.050
LVEF, %	65 ± 7	66 ± 7	63 ± 6	.057
≥55%	105 (95.5%)	60 (97%)	45 (94%)	.651
<55%	5 (4.5%)	2 (3%)	3 (6%)	—
MAPSE, mm	13 ± 2	14 ± 2	13 ± 2	.256
TAPSE, mm	24 ± 3	24 ± 3	23 ± 3	.942
SPAP, mmHg	23 ± 7	22 ± 8	24 ± 6	.209
E wave, cm/s	72 ± 21	75 ± 16	68 ± 25	.068
A wave, cm/s	67 ± 15	64 ± 15	70 ± 15	.060
E/A	1.1 ± 0.3	1.2 ± 0.4	1.0 ± 0.3	.002
DT, ms	209 ± 57	199 ± 47	222 ± 66	.036
E′, cm/s	10 ± 4	10 ± 4	9 ± 3	.107
E/E′	8.0 ± 2.7	7.6 ± 2.4	8.4 ± 3.1	.154
Diastolic filling pattern, n (%)				
Normal/abnormal relaxation/pseudonormal	63/45/2 (57%/41%/2%)	46/15/1 (74%/24%/2%)	17/30/1 (35%/63%/2%)	.001

A, late diastolic peak filling velocity; DT, deceleration time of early diastolic peak velocity; E, early diastolic peak filling velocity; E', tissue Doppler early diastolic septal mitral annular velocity; EF, ejection fraction; IVSd, end-diastolic wall thickness of interventricular septum; LAD, end-systolic left atrial diameter; LV, left ventricle; LVEDD, end-diastolic left ventricular dimension; LVMI, LV mass indexed to body surface area; LVPWd, end-diastolic thickness of LV posterior wall; MAPSE, average of mitral annular plane systolic excursion measured at the septal and lateral sites; RA, right atrium; RWT, relative wall thickness; SB, septal bulge; SPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; WT_Ratio, basal-septal to mid-septal wall thickness ratio.

segment was gradually decreased with increasing basal-septal WT.

ECG data were similar between groups except that left axis deviation was more frequently seen in SB group than in no-SB group (Table 6).

The interobserver absolute bias of basal- and mid-septal WT was 0.60 mm (95% CI 0.25–0.95) and 0.23 (95% CI −0.02 to 0.49), respectively. The intraobserver absolute bias of basal- and mid-septal WT was −0.10 mm (95% CI −0.47 to 0.27) and −0.17 mm (95% CI −0.45 to 0.11), respectively.

Discussion

In this cross-sectional study, we focused on a patient population without a history of AH and other cardiac diseases. In these patients, we searched for a SB as an early sign for cardiac remodeling. The main findings of the study are as follows: (1) the echocardiographic SB sign strongly predicted AH with sensitivity of 93% and specificity of 86%; (2) the SB in patients with AH is a very early sigh for hypertensive heart disease indicating remodeling of the LV with increasing regional WT and reduced local

Table 4
Logistic regression analysis of basal-septal to mid-septal wall thickness ratio (WT_Ratio) associated with AH defined by CET or ABMP

WT_Ratio	Chi Square	*P* Value	Nagelkerke R Square	Odds Ratio*	95% CI	*P* Value
Unadjusted	56.11	<.001	0.545	2.429	1.767–3.340	<.001
Adjusted†	57.40	<.001	0.576	2.319	1.664–3.233	<.001

ABPM, ambulatory blood pressure monitoring; AH, arterial hypertension; BMI, body mass index; BP, blood pressure; CET, cycle ergometer test; CI, confidence interval.

* The odds ratio for a 0.1 point change in WT_Ratio.

† Adjusted for age, gender, and BMI.

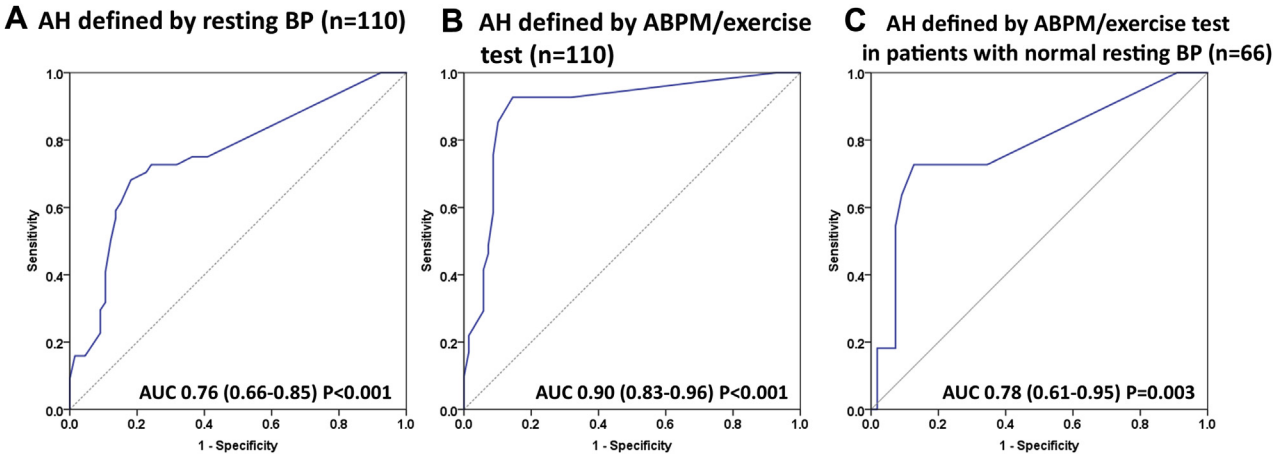

Figure 2. ROC analysis of the basal-septal to mid-septal wall thickness ratio (WT_ratio) for indicating AH defined by (A) resting BP (upper), by (B) CET or ABPM (lower), or defined by (C) CET/ABPM in patients with normal resting BP. Note that the diagnostic performance of WT_Ratio for AH by CET or ABPM was significantly better than by resting BP ($P = .018$). ABPM, ambulatory blood pressure monitoring; AH, arterial hypertension; AUC, area under the curve; BP, blood pressure; CET, cycle ergometer test; ROC, receiver operating characteristic.

myocardial function; (3) during clinical assessment, the diagnosis of AH is very unlikely in patients with normal echocardiographic findings and without a SB sign; and (4) in all patients with an accidental SB sign during echocardiography, a sophisticated diagnostic work up including resting BP measurement, ABPM, and CET for a potential AH should be initiated.

Data from the Framingham Heart study showed that the overall prevalence of SB was 1.5% in the general population.[18] Previous studies have suggested that hypertrophy in the basal portion of the intraventricular septum (ie, SB) in the elderly may represent a pattern of cardiac hypertrophy caused by hypertension.[18,31,32] In patients with AH, development of concentric LV hypertrophy is considered to be a typical adaptive process during long-lasting pressure overload.[33] Nevertheless, a number of patients with mild-to-moderate hypertension often exhibit normal WT and LV mass.[34] Some early hypertensive patients may only exhibit myocardial hypertrophy at the basal part of the septum, but with a normal LV WT elsewhere, thus, LV mass index might be still normal in these patients. Conforming to the aforementioned observations, our data also demonstrated that echocardiographic SB is frequently detected in AH patients at early disease stage with a high sensitivity (93%) and specificity (86%). Previous studies mostly studied established AH patients who had been suffering from high BP for years and decades. Differing from these studies, data from our study were derived from newly diagnosed AH patients who were unaware of their condition. These early AH patients largely presented with normal LV mass and normal global systolic and diastolic function except a distinct localized hypertrophy at the basal septum. Thus, SB seems be a specific localized structural remodeling in response to the elevated pressure load before the development of concentric hypertrophy at the early AH disease journey.

It is known that high-normal BP at resting BP assessment is indicative of increased risk for progression to hypertension compared to those with normal BP.[35] Nearly half of the patients with SB (46.9%) were found to have AH by CET and/or ABPM. In contrast, almost all patients without SB (90%) had no positive test for AH by CET or ABPM. SB strongly indicated the presence of AH not only in sustained hypertensive patients but also in ''prehypertensive'' patients.

It is to note that, of 44 patients with elevated resting BP, 14 patients tested negative for AH by either CET or ABPM (12 in no-SB group and 2 in SB group). These patients are clinically defined as ''white-coat'' hypertension. It is known that ''white-coat'' hypertension is a phenomenon in which patients show elevated BP in a clinical setting

Table 5
Longitudinal strain by speckle tracking imaging

	Total	No-SB	SB	*P* Value
	n = 110	n = 61	n = 49	
Septal wall longitudinal strain (%)				
Apical	24 ± 4	24 ± 5	25 ± 4	.823
Mid	20 ± 3	21 ± 3	19 ± 3	.006
Basal	16 ± 4	17 ± 4	14 ± 4	<.001
Lateral wall longitudinal strain (%)				
Apical	23 ± 5	23 ± 5	22 ± 5	.412
Mid	21 ± 4	22 ± 3	20 ± 4	.002
Basal	19 ± 4	19 ± 4	18 ± 4	.084
Global longitudinal strain (%)	20 ± 3	20 ± 3	19 ± 3	.008

SB, septal bulge.

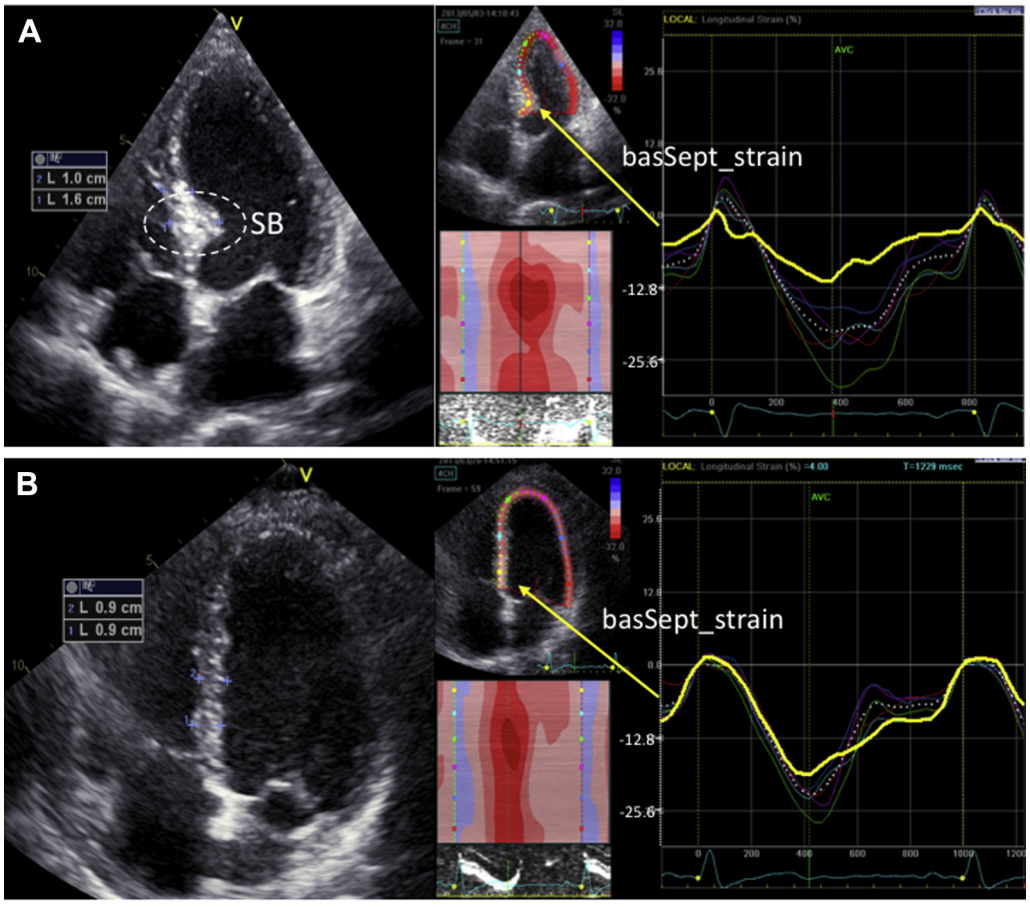

Figure 3. Examples of segmental longitudinal systolic strain curves derived from speckle tracing imaging in patients with (A) or without (B) septal bulge (SB).

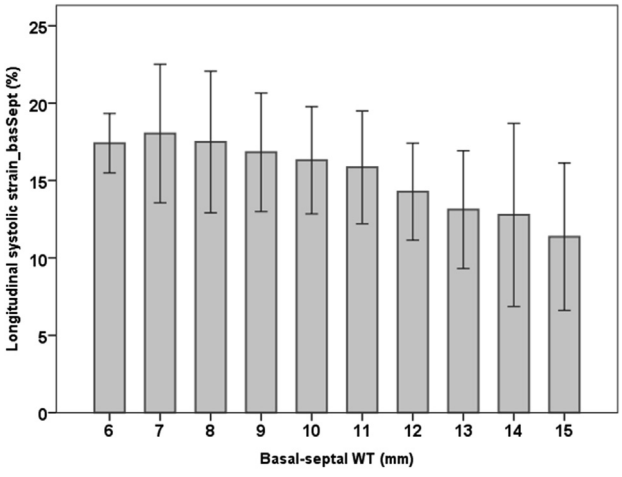

Figure 4. Association between regional longitudinal systolic strain and regional wall thickness (WT) at the basal-septal segment. Speckle tracking–derived longitudinal systolic strain at the basal-septal segment was gradually decreased with increasing basal-septal WT.

but not in other settings. ABPM or patient self-measurement using a home BP monitoring device is being increasingly used to differentiate those with ''white-coat'' hypertension from those with sustained hypertension. Our data showed a low prevalence of SB in these ''white-coat'' hypertension patients. Thus, during clinical BP measurement the presence or absence of an echocardiographic SB can be a useful feature to distinguish real AH from ''white-coat'' hypertension.

Masked hypertension is defined as normal resting BP in the clinic (<140/90 mm Hg), but elevated BP out of the clinic (ambulatory daytime BP or home BP > 135/85 mm Hg).[36,37] It is known that even masked hypertension can be associated with end-organ damage.[37] Twenty-four–hour ABPM provides multiple, objective BP measurements in the patient's own environment over a full circadian period. Meanwhile, exercise testing has being increasingly recognized as a useful tool for cardiovascular risk prediction of asymptomatic patients with normal or borderline BP.[38] Exercise test can be used to evaluate prehypertensive stages, to characterize hypertension, and to assess tolerance to exercise as well as the efficacy of antihypertensive therapies.[39,40]

Table 6
Resting and exercise electrocardiography

	No-SB	SB	*P* Value
	n = 62	n = 48	
Heart rate, beats/min	69 ± 9	72 ± 11	.210
Sinus rhythm	60 (98%)	48 (100%)	.373
LV Sokolow index, mV	1.9 ± 0.7	1.9 ± 0.6	.966
Mean electrical axis			.027
Normal axis	45 (73%)	25 (52%)	
Left-axis deviation	17 (27%)	23 (48%)	
Right-axis deviation	0 (0%)	0 (0%)	
ST-segment depression at rest	0 (0%)	1 (2%)	.262
ST-segment depression during exercise	2 (3%)	4 (9%)	.236

LV, left ventricle; SB, septal bulge.

In the present study, 11 (16.7%) patients could be defined as masked hypertension. Interestingly, 8 (72.7%) of these patients exhibited SB sign. These findings further support the diagnostic value of echocardiographic SB sign for AH. In addition, it proposes that measurement of BP with appropriate tools is essential to unmask hypertension.

AH results in a permanent pressure overload of the LV. In patients with hypertension, the LV myocardium compensates for this increased systolic wall stress by developing hypertrophy. Regional wall stress of LV wall is inhomogeneous according to the irregular curvature within the nonspheric LV.[41] Owing to the largest local radius of the LV curvature at the basal septum, wall stress is highest there. Because hypertrophy is directly related to wall stress the basal septal segment usually develops first the characteristic bulge. In newly diagnosed hypertensive patients, this basal SB is especially prominent as the rest of the LV is not yet hypertrophic.[42] Previous studies have shown that hypertrophic tissue induced by AH is associated with decreased myocardial efficiency and perfusion reserve.[43] Thus, the decreased deformation at basal-septal segment in AH (assessed by speckle tracking imaging) might be caused by myocardial hypertrophy with a suboptimal perfusion of the subendocardium.[44–46]

In previous studies, SB was defined as 50% greater than the thickness of the mid septal wall (mm) at end-diastolic phase.[32] In the present study, we decided to use the strict criterion of a minimal difference of 2 mm in WT as a definition for SB to be very precise and to avoid missing patients with this potential imaging sign for hypertension. It is relatively difficult to measure in clinical routine. However, the present study was aimed as proof of concept study. Thus, further larger multicenter studies have to confirm the current findings. As in some patients the SB was quite prominent, we cannot completely rule out that these hearts suffer from hypertrophic cardiomyopathy.

Screening started from the echocardiographic assessment in the present study. Thus, the ''real normal'' population was not included in this cohort. The prevalence of SB reported in this cohort therefore did not reflect that of the general population.

In addition, it is to note that the ABPM procedure and AH diagnosis criteria in the present study were based on the JNC 7 report,[1] not on the ABPM recommendation of 2013.[47] This point needs to be cared by interpredating present results.

In clinical practice, echocardiographic SB with a normal LV mass is often not considered as a pathologic sign by clinicians. Our data suggest that SB is a reliable and sensitive echocardiographic sign, highly suggestive for AH patients at early disease stage. Furthermore, SB could be considered as a sign reflecting the early response to high BP load even appearing in prehypertensive status. Until now, ABPM and exercise BP assessment have not been included in the routine screen for confirming AH because of reimbursement issues, equipment expenses, and time efforts to train patients in monitor use. The present study suggests that the presence of SB on echocardiography could be an easy but helpful indicator in asymptomatic AH patients and thus to initiate sophisticated diagnostics for AH. Absence of SB is suggestive of ''white-coat'' hypertension in patients with elevated resting BP. In patients with SB sign but normal resting BP, performing CET and ABPM might be valuable to detect masked hypertension.

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