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ORIGINAL ARTICLE

Strain/strain rate imaging of impaired left atrial function in patients with metabolic syndrome

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Left ventricular (LV) dysfunction has been demonstrated in patients with metabolic syndrome (MetS). However, alterations in left atrial (LA) function in MetS are unknown. We aimed to use strain/strain rate (SR) imaging to investigate the effect of MetS on LA function. A total of 177 MetS patients and 156 normal subjects underwent echocardiography. Strain and SR tissue Doppler imaging values were used to evaluate LA function. Partial correlation and multiple stepwise regression analyses were used to determine the risk factors for impaired LA function. Compared with the controls, the MetS patients showed significantly lower levels of mean strain, mean peak systolic SR and mean peak early diastolic SR ($P<0.001$ for all), with no difference in the mean peak late diastolic SR. Central obesity, hypertension, dyslipidemia and LV diastolic abnormality were independent risk factors for impaired LA function. LA function was impaired in patients with MetS as a result of metabolic disturbance and LV diastolic abnormality. SR imaging is reliable in assessing LA function in MetS patients.
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Keywords: left atrial function; left ventricular diastolic abnormality; metabolic syndrome; strain

INTRODUCTION

Large population-based studies have shown that metabolic syndrome (MetS), a well-described constellation of atherogenic risk factors, including obesity, hypertension, insulin resistance and dyslipidemia, increases the risk of cardiovascular diseases and all-cause mortality.[1–4] Recently, MetS has been associated with left ventricular (LV) hypertrophy, LV diastolic dysfunction and left atrial (LA) enlargement.[5–7] The left atrium modulates LV filling and cardiovascular performance during every phase. Thus, the left atrium is at the intersection of MetS and LV performance.

Because the incidence of paroxysmal atrial fibrillation and atrial flutter is higher in MetS patients without structural heart diseases,[8] investigating alterations in the LA structure and function in these patients is of interest. However, whether MetS itself or the consequent LV diastolic dysfunction is the cause of alterations of the left atrium is unknown. Therefore, we aimed to assess alterations in the LA function in patients with MetS using strain/strain rate (SR) imaging and to determine the leading risk factors and potential mechanisms.

METHODS

Study population

We recruited 177 consecutive patients with MetS (75 males with a mean age of 53.7 ± 8.5 years, range 26–74), with cardiovascular risk factors (obesity, hypertension, glucose tolerance/diabetes mellitus and dyslipidemia) and no previous history or clinical evidence of heart failure or overt coronary artery disease. We also enrolled 156 age- and sex-matched normal subjects (57 males with a mean age of 52.7 ± 8.7 years, range 35–85 years) without cardiovascular disease, hypertension or diabetes mellitus. All the subjects were in sinus rhythm. At inclusion, all the subjects underwent a thorough review of their medical history, clinical examination and electrocardiography for the detection of clinical events. Informed consent was obtained from all subjects on the basis of a protocol approved by the Ethics Committee of QiLu Hospital, Shandong University, China.

Clinical assessment

We obtained details of age, sex, weight and height, and heart rate; body mass index was calculated as body weight in kilograms divided by height in meters squared. Waist circumference was measured at the level of the umbilicus. Systolic and diastolic blood pressure (BP) readings were obtained using a mercury sphygmomanometer and auscultatory methods. MetS was diagnosed according to the criteria in the 2005 guidelines of the International Diabetes Federation: (1) central obesity (waist circumference $\geqslant 90$ cm for men and $\geqslant 80$ cm for women) and (2) the presence of two or more of the following: systolic BP $\geqslant 130$ mm Hg or diastolic BP $\geqslant 85$ mm Hg or receiving antihypertensive medication, a triglyceride (TG) level $\geqslant 150$ mg dl^{-1} or receiving specific treatment for this lipid abnormality, high-density lipoprotein cholesterol

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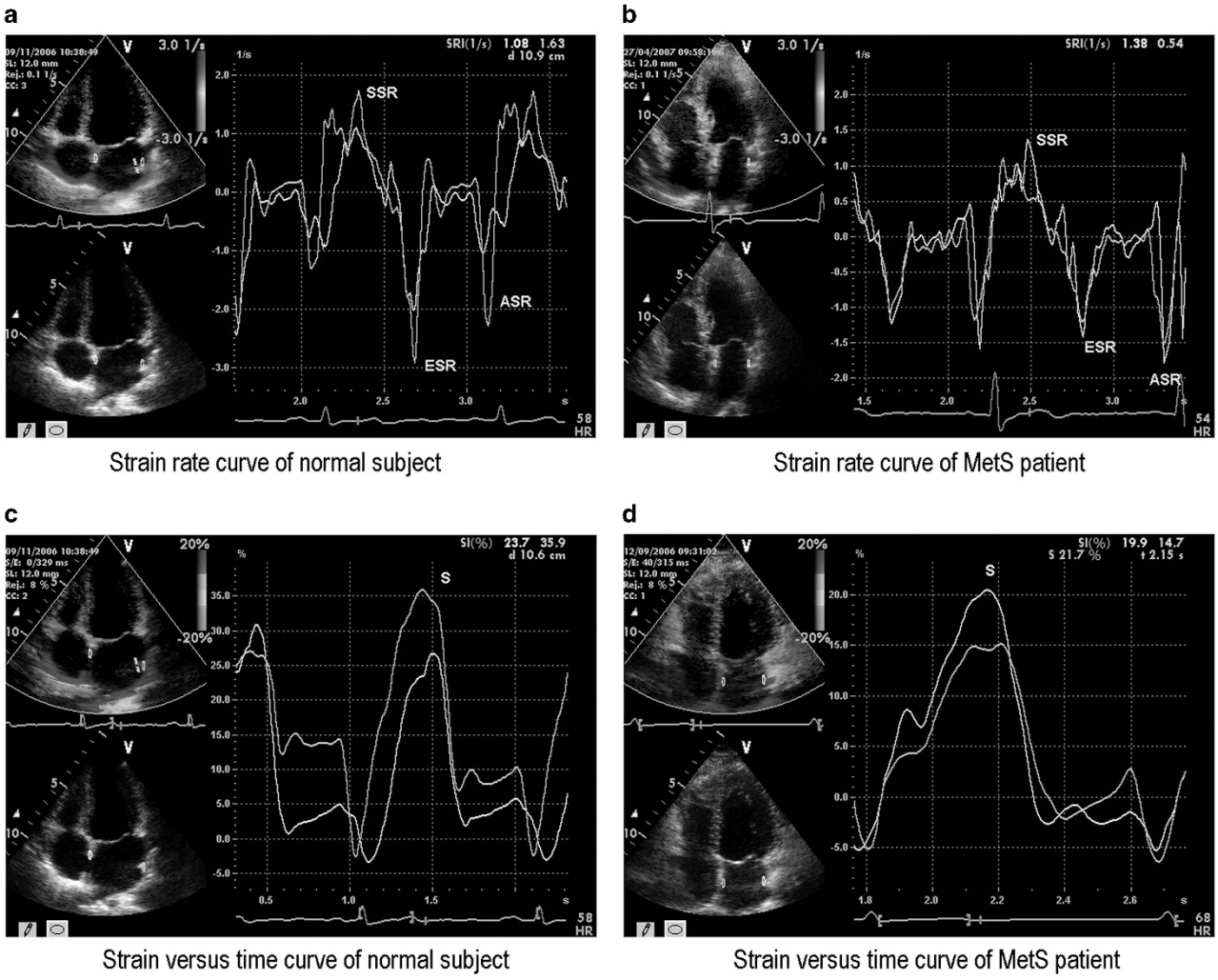

Figure 1 Strain rate/strain *vs.* time curve for one cardiac cycle obtained from the apical four-chamber view (two curves with different colors depict each myocardial segment). (**a**) Strain rate curve of normal subjet. (**b**) Strain rate curve of MetS patient. (**c**) Strain versus time curve of normal subject. (**d**) Strain versus time curve of MetS patient. A full color version of this figure is available at *Hypertension Research* online.

(HDL)-C $< 40\ mg\ dl^{-1}$ for men or $< 50\ mg\ dl^{-1}$ for women, fasting glucose $\geqslant 100\ mg\ dl^{-1}$ or a previous diagnosis of type 2 diabetes mellitus.

Biochemical assessment

Blood was drawn after the participants had fasted overnight. Plasma levels of total cholesterol, HDL-C, low-density lipoprotein cholesterol (LDL-C), TGs and fasting blood glucose (FBG) were measured using standard laboratory techniques. After centrifugation, the fasting serum insulin (FINS) was determined using a radio-immunoassay kit (Dongya, Beijing, China). Homeostatic model assessment-insulin resistance index (HOMA-IRI) was calculated using the homeostasis model assessment method (fasting insulin in microunits per milliliter multiplied by fasting glucose in millimoles per liter divided by 22.5).[9] The insulin sensitivity index was calculated as follows: $ISI = -\ln(FBG \times FINS)$.[10]

Echocardiography examination

A commercially available ultrasound machine (Vivid 7 Dimension; General Electric Medical Systems, Horten, Norway) with a 2.5-MHz variable-frequency transducer was used for all the echocardiographic studies. Standard echocardiographic views, including parasternal long-axis and apical four-, three- and two-chamber views, were obtained in two-dimension and color tissue velocity imaging modes with the subjects lying in the left lateral decubitus position. The LV dimensions and LV ejection fraction (%) were measured in two-dimension-guided M mode below the mitral valve leaflets in the parasternal long-axis view. LV end-diastolic diameters and septal and LV posterior end-diastolic wall thickness were measured as recommended by the American Society of Echocardiography. LV mass was calculated using the formula proposed by Devereux *et al.*[11] and normalized for body surface area (LV mass index, $g\ m^{-2}$). The LA dimension was defined as the largest distance between the posterior aortic and the atrial walls in the parasternal long-axis view during systole. The final values were obtained from the average of 3–5 measurements. The LA volume was calculated by the ellipsoid method (LA volume $= 4\pi/3$ (L/2) (D1/2) (D2/2)) and normalized for the body surface area (LA volume index, $ml\ m^{-2}$). D1 was the LA anteroposterior diameter acquired from the parasternal long-axis. D2 was the LA medial-lateral dimension from the parasternal short-axis. L was the LA long-axis from the apical four-chamber.

Transmitral flow profile was assessed using two-dimension-guided pulsed-wave Doppler in the apical four-chamber view by positioning a 3-mm-sized sample volume between the tips of the mitral leaflets in diastole and recording at a sweep velocity of $100\ mm\ s^{-1}$. Mitral flow parameters included peak velocities during early diastole (E) and late diastole (A) as well as their ratio (the E/A ratio).

Tissue doppler imaging and strain/SR measurements

Color tissue Doppler images from the apical two-chamber, four-chamber and long-axis views were recorded, with frame rates between 90 and 150 frames per second automatically changed by the sector width. Three to five cardiac cycles were recorded in each cine loop. Three cine loops were recorded for each patient and saved digitally on a magneto-optical disk (MO-4.8GB; IMATION, Tokyo, Japan) for later analysis offline.

Myocardial Doppler velocity profile signals were reconstructed off-line from the tissue velocity imaging color images. In the apical two-chamber, four-chamber and long-axis views, the regional analysis consisted of placing the region-of-interest cursor at the corners of the mitral annulus at the septum, anterior, lateral, posterior and inferior walls. The strain and SR curves were assessed in the inner half of the myocardium on the basal and mid segments of the left atrium at the septum, anterior, lateral, posterior and inferior walls in the apical views. A sample volume 2.0 mm wide and 6.0 mm long was used in all the studies. The sample volume was manually tracked frame by frame to ensure that it maintained the same position within the myocardium throughout the cardiac cycle. Thus, curves for tissue velocity *vs.* time, strain *vs.* time, and SR *vs.* time (Figure 1) were generated from these regions of interest. The tissue velocity imaging and SR curves were typical triphasic curves, but the strain curves were monophasic. We measured (Vs) peak systolic diastolic velocity, peak early diastolic velocity (Ve), peak late diastolic velocity (Va), peak strain (S), peak systolic SR (SSR), peak early diastolic SR (ESR) and peak late diastolic SR (ASR) in each segment of the five LA walls (septum, lateral, posterior, anterior and inferior). The average values of Vs, Ve, Va, S, SSR, ESR and ASR were defined as Vs_{global}, Ve_{global} and Va_{global} and the mean S, SSR, ESR and ASR, respectively.

Table 1 Clinical characteristics of controls and patients with metabolic syndrome

Variables	*Controls (n = 156)*	*MetS (n = 177)*
Clinical characteristics		
Male gender	57(36.54%)	75(42.37%)
Age (years)	52.69 ± 8.69	53.65 ± 8.51
Systolic BP (mm Hg)	115.88 ± 9.77	150.74 ± 22.07***
Diastolic BP (mm Hg)	75.47 ± 6.48	94.68 ± 13.93***
PP (mm Hg)	40.41 ± 8.47	56.00 ± 15.52***
HR (prm)	78.54 ± 11.07	80.26 ± 9.81
BMI ($kg\,m^{-2}$)	24.50 ± 2.78	29.08 ± 4.36***
BSA (m^2)	1.68 ± 0.15	1.87 ± 0.23***
Waist circumference (cm)	84.44 ± 8.00	98.01 ± 10.46***
Waist-to-hip ratio	0.86 ± 0.06	0.92 ± 0.06***
Laboratory examinations		
Cholesterol ($mmol\,l^{-1}$)	4.61 ± 0.82	5.41 ± 1.08***
Triglyceride ($mmol\,l^{-1}$)	1.09 ± 0.49	2.38 ± 1.96***
HDL-C ($mmol\,l^{-1}$)	1.53 ± 0.34	1.26 ± 0.34***
LDL-C ($mmol\,l^{-1}$)	2.91 ± 0.70	3.62 ± 0.93***
FBG ($mmol\,l^{-1}$)	4.88 ± 0.58	6.55 ± 2.55***
FINS ($uU\,mol\,l^{-1}$)	10.75 ± 4.67	20.34 ± 10.70***
ISI	−3.87 ± 0.46	−4.73 ± 0.60***
HOMA-IRI	2.38 ± 1.22	6.03 ± 4.31***
Echocardiographic parameters		
LVEF	0.65 ± 0.05	0.66 ± 0.06
LA dimension (mm)	31.16 ± 2.62	35.47 ± 3.46***
LA volume(ml)	40.19 ± 11.33	58.95 ± 20.89***
LA volume index ($ml\,m^{-2}$)	24.22 ± 7.25	31.92 ± 11.71***
IVSd (mm)	9.79 ± 1.06	11.76 ± 1.51***
LVPWd (mm)	8.97 ± 0.99	10.39 ± 1.21***
LVEDd (mm)	42.85 ± 4.29	44.34 ± 5.01**
LV mass (g)	131.58 ± 30.73	174.95 ± 43.99***
LV mass index ($g\,m^{-2}$)	78.19 ± 14.81	94.39 ± 21.58***
Mitral E ($cm\,s^{-1}$)	79.56 ± 14.74	77.34 ± 18.10
Mitral A ($cm\,s^{-1}$)	68.23 ± 14.62	85.06 ± 18.35***
E/A ratio	1.21 ± 0.30	0.93 ± 0.24***
Vs_{global} ($cm\,s^{-1}$)	6.54 ± 1.76	5.24 ± 1.48***
Ve_{global} ($cm\,s^{-1}$)	9.00 ± 2.61	6.81 ± 1.87***
Va_{global} ($cm\,s^{-1}$)	6.86 ± 2.15	7.27 ± 2.00
Ve_{global}/Va_{global} ratio	1.50 ± 0.81	0.98 ± 0.40***
E/Ve_{global} ratio	9.359 ± 2.73	11.92 ± 3.85***

Abbreviations: BMI, body mass index; BP, blood pressure; BSA, body surface area; FBG, fast blood glucose; FINS, fast insulin; HDL-C, high-density lipoprotein cholesterol; HOMA-IRI, insulin resistant index; HR, heart rate; ISI, insulin sensitive index; IVSd, septal end-diastolic wall thickness; LA, left atrial; LDL-C, low-density lipoprotein cholesterol; LV, left ventricular; LVEDd, LV end-diastolic diameter; LVPWd, LV posterior end-diastolic wall thickness; Mitral A, peak velocities during late diastole; Mitral E, peak velocities during early diastole; PP, pulse pressure; Va_{global}, mean late diastolic peak tissue velocity; Ve_{global}, mean early diastolic peak tissue velocity; Vs_{global}, mean systolic peak tissue velocity. Data are presented as mean value ± s.d. $^{**}P<0.01$, $^{***}P<0.001$ *vs.* controls.

Statistical analyses

Statistical analyses involved the use of SPSS 13.0 (SPSS, Chicago, IL, USA). The data are presented as the mean ± s.d. for continuous variables and as proportions for categorical variables. Differences in continuous variables between the two groups were assessed by independent sample Student's *t*-tests. Categorical variables were analyzed by the χ^2-test. The correlation between two variables was tested using Pearson's correlation coefficient. The independent correlation of LA function with metabolic factors and LV diastolic function was investigated using partial correlation analysis. Variables with $P<0.10$ in the univariate analysis were entered into the multivariate model with a stepwise regression analysis. Bland–Altman plots were used to assess intraobserver and interobserver reproducibility. One of the investigators (Ning-ning Fang) repeated the VVI (Velocity Vector Imaging) and obtained strain data for 10 randomly selected patients at two time points to determine the intraobserver reproducibility. Another investigator (Hui-ping Gong) independently obtained VVI data for the same 10 patients to determine interobserver reproducibility. The mean bias and limits of agreement (1.96 ± s.d.) from the Bland–Altman plot are presented for the intraobserver and interobserver reproducibility. A $P<0.05$ was considered statistically significant.

RESULTS

Clinical characteristics

The general characteristics of the study population are summarized in Table 1. The controls and MetS subjects did not differ in age or sex. As expected, the MetS patients had significantly larger waist circumference; higher body mass index, HOMA-IRI, BP and levels of TGs and LDL-C, insulin, and fasting glucose; and lower HDL-C levels and ISI as compared with controls.

Echocardiographic findings

The echocardiographic characteristics of the participants are listed in Table 1. Compared with the controls, the MetS patients showed significantly greater septal and posterior wall thickness, larger LA end-diastolic dimensions and LA volume, higher LA volume and LV mass indices, greater LV mass and peak velocity of the mitral A wave, and a higher E/Ve_{global} ratio but smaller E/A, Ve_{global} and Ve_{global}/Va_{global} ratios.

Strain and SR Parameters of LA in MetS

The mean S and SSR, considered indicators of the LA reservoir function, were significantly lower for the MetS patients than for the controls. The mean ESR, an indicator of the LA conduit function, was significantly lower for the MetS patients than for the controls. The controls and MetS patients did not differ in mean ASR, an indicator of LA booster function (Table 2).

Table 2 Comparison of strain and strain rate parameters of controls and patients with metabolic syndrome (MetS)

Variables	*Controls (n = 156)*	*MetS (n = 177)*
Mean S (%)	27.89 ± 5.11	19.31 ± 4.78***
Mean SSR (s^{-1})	1.56 ± 0.29	1.12 ± 0.30***
Mean ESR (s^{-1})	−1.60 ± 0.42	−0.97 ± 0.30***
Mean ASR (s^{-1})	−1.42 ± 0.26	−1.47 ± 0.31

Abbreviations: ASR, peak late diastolic strain rate; ESR, peak early diastolic strain rate; MetS, metabolic syndrome; S, strain; SSR, peak systolic strain rate.
Data are presented as mean value ± s.d.
***$P<0.001$ *vs.* controls.

Relationship between LA strain/SR parameters and clinical and echocardiographic variables

After controlling for the variables that describe left ventricular diastolic function (Ve_{global} and the Ve_{global}/Va_{global} and E/Ve_{global} ratios), partial correlation analysis to investigate the relationship between LA function and metabolic factors revealed that the mean S was significantly correlated with systolic BP; diastolic BP; pulse pressure; waist circumference; waist-to-hip ratio; cholesterol, TG, LDL-C levels; FBG; FINS; ISI and HOMA-IRI. The mean SSR was significantly correlated with age; systolic BP; diastolic BP; pulse pressure; waist circumference; waist-to-hip ratio; cholesterol; TG, HDL-C and LDL-C levels; FBG; FINS; ISI and HOMA-IRI. The mean ESR was significantly correlated with age; systolic BP; diastolic BP; pulse pressure; waist circumference; waist-to-hip ratio; cholesterol, TG, HDL-C and LDL-C levels; FBG; FINS; ISI and HOMA-IRI (Table 3).

After controlling for heart rate and metabolic variables (systolic BP; diastolic BP; pulse pressure; waist circumference; waist-to-hip ratio; cholesterol, TG and LDL-C levels, FBG; FINS; ISI and HOMA-IRI), partial correlation analysis to investigate the relationship between LA function and LV diastolic function revealed that the mean S and mean SSR were significantly correlated with Ve_{global} and E/Ve_{global} ratio, and the mean ESR was significantly correlated with Ve_{global} and the Ve_{global}/Va_{global} and E/Ve_{global} ratios (Table 4).

The significant association of MetS with LA function was confirmed by linear stepwise multiple regression analyses (Table 5). Systolic BP, Ve_{global}, ISI, cholesterol level and waist-to-hip ratio were significant determinants of the mean S, and Ve_{global}, systolic BP, cholesterol level, age and waist circumference were significant determinants of the mean ESR in the multivariate model, whereas the mean SSR was significantly correlated with systolic BP, cholesterol level, Ve_{global}, ISI, age and HDL-C level.

Intraobserver and interobserver reproducibility

Intraobserver and interobserver reproducibility for the LA mean ESR derived from VVI is presented in Figure 2. The mean intraobserver bias was 0.9 (limits of agreement, −0.25–0.26) for the LA mean ESR. The mean interobserver bias was 0.3 (limits of agreement, −0.16–0.23) for the LA mean ESR.

DISCUSSION

Our study is the first to evaluate LA function in MetS patients by strain/SR imaging. We found that the LA reservoir and conduit functions were impaired and that the booster function was maintained. In addition, the main components of MetS—central obesity, hypertension, dyslipidemia and decreased ISI—were independent risk factors for impaired LA function.

Table 3 Partial correlation analysis of strain/strain rate parameters of the left atrium and clinical characteristics after controlling for variables describing left ventricular diastolic function

	Partial correlation coefficients		
Variables	*Mean S*	*Mean SSR*	*Mean ESR*
Age	−0.073	−0.137*	0.244***
Systolic BP	−0.426***	−0.402***	0.403***
Diastolic BP	−0.352***	−0.304***	0.303***
PP	−0.340***	−0.351***	0.352***
Waist circumference	−0.346***	−0.280***	0.346***
Waist-to-hip ratio	−0.315***	−0.250***	0.327***
Cholesterol level	−0.225***	−0.234***	0.313***
Triglyceride level	−0.205***	−0.142*	0.217***
HDL-C level	0.099	0.162**	−0.129*
LDL-C level	−0.218***	−0.254***	0.299***
FBG	−0.227***	−0.202**	0.206***
FINS	−0.269***	−0.217***	0.179**
ISI	0.382***	0.303***	−0.284***
HOMA-IRI	−0.268***	−0.234***	0.193**

Abbreviations: BP, blood pressure; ESR, peak early diastolic strain rate; FBG, fast blood glucose; FINS, fast insulin; HDL-C, high-density lipoprotein cholesterol; HOMA-IRI, insulin resistant index; ISI, insulin sensitive index; LDL-C, low-density lipoprotein cholesterol; PP, pulse pressure; S, strain; SSR, peak systolic strain rate.
**$P<0.01$, ***$P<0.001$.

Table 4 Partial correlation analysis of strain/strain rate parameters of the left atrium and variables for left ventricular diastolic function after controlling for metabolic variables and heart rate

	Partial correlation coefficients		
Variables	*Mean S*	*Mean SSR*	*Mean ESR*
Ve_{global}	0.376***	0.243***	−0.559***
Ve_{global}/Va_{global} ratio	0.108	0.067	−0.348***
E/Ve_{global} ratio	−0.280***	−0.166***	−0.315***

Abbreviations: ESR, peak early diastolic strain rate; S, strain; SSR, peak systolic strain rate; Va_{global}, mean late diastolic peak tissue velocity; Ve_{global}, mean early diastolic peak tissue velocity.
***$P<0.001$.

Impact of MetS on the cardiovascular system

MetS is a cluster of atherogenic risk factors, including abdominal obesity, hypertension, insulin resistance, dyslipidemia, proinflammation and a prothrombotic state. Several studies investigating LV structure and function in patients with MetS demonstrated that the syndrome is associated with LV hypertrophy and LV diastolic dysfunction in hypertensive patients as well as in the general population.[5–7] In the present study, patients with MetS showed significant alteration of LV geometry and function as characterized by LV hypertrophy and abnormal early diastolic LV relaxation, although LV systolic function was normal.

Strain and SR imaging in evaluating LA function

The development of novel echocardiographic techniques, such as tissue Doppler imaging, has enhanced the ability to assess regional myocardial function noninvasively.[12–14] One such technique, strain/SR imaging, has recently emerged as a method to quantify LA, LV and RV regional myocardial function independent of cardiac rotational motion and a tethering effect[15,16] as well as to enable quantitative assessment of LA function in patients with paroxysmal atrial fibrillation and atrial

septal defect.[17–19] LA function contributes greatly to LV filling through the following three components: a reservoir phase during systole, a conduit phase during diastole and an active contractile component (when sinus rhythm is present) during late diastole. Previous studies have demonstrated that strain, SSR and LA deformation during systole could be used as indices of the LA reservoir function in collecting blood from the pulmonary vein influx to the left atrium and that the mean ESR was assessed in a phase when the left atrium works mainly as a conduit and could be used as an index of LA myocardial conduit function. The efficacy of strain/SR imaging, however, has not been determined in patients with MetS. Our study of strain/SR imaging revealed that the LA reservoir and conduit functions were seriously impaired in MetS patients, as reflected by a decreased mean S, SSR and ESR.

Table 5 Multiple stepwise regression analysis of strain/strain rate parameters of the left atrium and clinical characteristics/ echocardiographic parameters

Variables	*β*	R^2	P-*value*
Mean S			
Systolic BP	−0.286	0.308	0.000
Ve_{global}	0.276	0.410	0.000
ISI	0.174	0.452	0.001
Cholesterol level	−0.120	0.467	0.009
Waist-to-hip ratio	−0.120	0.478	0.015
Mean SSR			
Systolic BP	−0.300	0.263	0.000
Cholesterol level	−0.161	0.312	0.002
Ve_{global}	0.126	0.341	0.026
ISI	0.153	0.358	0.006
Age	−0.127	0.369	0.014
HDL-C level	0.107	0.379	0.034
Mean ESR			
Ve_{global}	−0.363	0.444	0.000
Systolic BP	0.219	0.540	0.000
Cholesterol level	0.175	0.588	0.000
Age	0.196	0.641	0.000
Waist circumference	0.151	0.649	0.009

Abbreviations: BP, blood pressure; ESR, peak early diastolic strain rate; HDL-C, high-density lipoprotein cholesterol; ISI, insulin sensitive index; S, strain; SSR, peak systolic strain rate; Ve_{global}, mean early diastolic peak tissue velocity.

Impact of MetS on LA reservoir and conduit function

The individual components of MetS are associated with abnormal cardiac structure and function. These components tend to have synergistic effects on cardiac functions. Reilly *et al.*[20] demonstrated that the effect of MetS on the cardiovascular system is greater than the sum of its components. In our study, we found that impaired LA function in patients with MetS was independently associated with hypertension, central obesity, dyslipidemia and insulin resistance.

Obesity, particularly central obesity, is an important risk factor for cardiac dysfunction independent of the other components of MetS.[21] Chiew[22] described a potential pathophysiologic mechanism for the cardiomyopathy of obesity that begins with increased cardiac output, enhanced LV volume and enlarged LA diameter. Adipose tissue might contribute to circulating angiotensin II,[23] which promotes myocardial tissue growth and influences the aldosterone level, which in turn mediates myocardial fibrosis. Myocardial fibrosis in moderate and severely obese subjects was confirmed by myocardial biopsy.[24] Our results indicate that central obesity contributes to decreased LA reservoir and conduit function.

Because the impact of hypertension on cardiac structure and function has been widely studied in MetS cohorts,[25] the alterations in LA function in patients with hypertension have been thoroughly demonstrated.[15,26] Kokubu *et al.*[26] showed that the impaired LA function in hypertensive patients might be attributable to LA myocardial fibrosis, as shown in an animal study.[27] We found that systolic BP is the independent factor most responsible for decreased LA reservoir and conduit function.

Although the underlying mechanism of MetS that is responsible for increased cardiovascular risk has not been elucidated, the possibilities were reviewed by Deedwania,[28] who concluded that insulin resistance is the basic mechanism. The alterations in myocardial substrate metabolism are related to reduced myocardial contractile dysfunction in patients with insulin resistance and diabetes.[29,30] Therefore, insulin resistance in MetS and type 2 diabetes patients might have an important role in cardiac dysfunction. We found a significant relationship between LA function and ISI.

Interestingly, we found a weak but independent relationship between LA function and dyslipidemia, which has rarely been

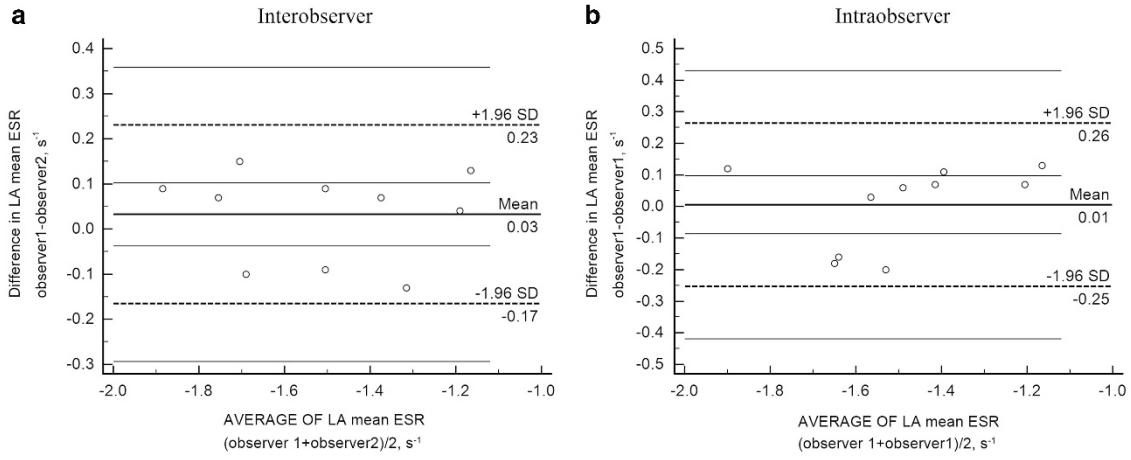

Figure 2 Intraobserver and interobserver reproducibility for the VVI-derived and LA mean strain rates. (**a**) The mean bias interobserver was 0.3 (limits of agreement, –0.16 to 0.23,) for LA mean ESR. (**b**) The mean bias intraobserver was 0.9 (limits of agreement, –0.25 to 0.26,) for LA mean ESR.

demonstrated. Dyslipidemia, an independent risk factor for increased cardiovascular mortality and mobility,[31,32] can cause vascular endothelial dysfunction, leading to abnormal myocardium infusion and reconstruction of myocardial cells and the interstitium.[33] Therefore, dyslipidemia may have harmful effects on LA function, although the exact mechanisms remain unclear.

The Relationship between LV diastolic function and LA function in MetS

LA function has an important role in LV filling, particularly in patients with impaired diastolic function. LA function is directly influenced by LV diastolic function. Compared with the controls, the MetS patients in our study showed decreased early diastolic peak tissue velocity of the mitral valve annulus (Ve_{global}), a lower ratio of early to late diastolic peak tissue velocity (Ve_{global}/Va_{global}) and a higher E/Ve_{global} ratio reflecting LV diastolic function, which is consistent with a previous hypothesis that an LV diastolic abnormality accompanies MetS. Grandi *et al.*[34] showed that only LV diastolic function was reduced in MetS. Therefore, the alteration in LA function might be attributable to abnormal blood flow from the left atrium to the left ventricle consequent to increased LV stiffness. The association of LV diastolic function with the parameters of LA function showed that LV diastolic function led to decreased LA reservoir and conduit functions; this was confirmed by linear stepwise multiple regression analyses and partial correlation analysis after controlling for age, heart rate and metabolic variables.

Alteration of LA systolic function in MetS

The mean ASR was negative during late diastole, which indicates shortening of the LA wall. We found no significant difference in the mean ASR between the control and MetS groups, which indicates that MetS had no effect on LA myocardial contractility. Similarly, Kokubu *et al.*[25] found no significant difference in LA booster function in hypertensive patients using SR imaging, in contrast to conventional echocardiographic imaging. Possible reasons for the discrepant results might be that SR imaging reflects regional LA myocardial functions rather than global functions. Compared with the conventional echocardiographic parameters (that is, the LA myocardium and interstitium fibrosis), SR imaging might be able to detect these subtle changes in the LA wall.

Our study has some limitations. Tissue Doppler imaging measurements are angle-dependent, which might influence the accuracy of the results. In our study, we performed strain/SR imaging measurements, keeping the angle between the ultrasound beam and the LA longitudinal axis as small as possible ($<30°$) to eliminate error. There was no appropriate stress testing, so patients with subtle coronary artery disease might not have been excluded. In addition, because we examined a relatively small number of patients with MetS, our observations require confirmation by a prospective large-scale population study.

In summary, patients with MetS have impaired LA function, and SR imaging is reliable in assessing it. Central obesity, hypertension, dyslipidemia and decreased ISI are independent risk factors for impaired LA function; however, the precise mechanisms remain to be elucidated.

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