Original Article

Interaction effect of hypertension and obesity on left atrial phasic function: a three-dimensional echocardiography study

Rui Zhang, Cunying Cui, Shuojing Wang, Ying Wang, Ruijie Liu, Lin Liu

Department of Ultrasound, People's Hospital of Zhengzhou University, Henan Provincial People's Hospital, Fuwai Central China Cardiovascular Hospital, Zhengzhou, China

Contributions: (I) Conception and design: R Zhang, C Cui, L Liu; (II) Administrative support: L Liu; (III) Provision of study materials or patients: S Wang, Y Wang, R Liu; (IV) Collection and assembly of data: R Zhang, S Wang; (V) Data analysis and interpretation: R Zhang, C Cui, S Wang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Lin Liu, MD, PhD. Department of Ultrasound, People's Hospital of Zhengzhou University, Henan Provincial People's Hospital, Fuwai Central China Cardiovascular Hospital, 7 Weiwu Road, Jinshui District, Zhengzhou 450003, China. Email: liulin@zzu.edu.cn.

Background: Hypertension (HT) and obesity often coexist and contribute to left atrial (LA) dysfunction. The present study aimed to compare LA function in hypertensive individuals and control participants with different body mass index (BMI) categories and to explore whether there is an interaction effect between HT and obesity on LA function.

Methods: In this cross-sectional study, a total of 258 individuals (145 hypertensive and 113 non-hypertensive patients) were prospectively enrolled from Fuwai Central China Cardiovascular Hospital from September 2020 to November 2021. Hypertensive and non-hypertensive patients were both divided into three study subgroups (n=35 per group) according to their BMI: normal weight (BMI 18.5–<25 kg/m^2), overweight (BMI 25–<30 kg/m^2), and obesity (BMI ≥30 kg/m^2) groups. LA volume and strain parameters were obtained using three-dimensional echocardiography.

Results: A significant interaction effect between HT and obesity on LA function was observed [$P_{Interaction}$ =0.04, 0.03, 0.005, 0.01, and 0.002 for LA ejection fraction (LAEF), LA passive ejection fraction (LAPEF), LA active ejection fraction (LAAEF), LA reservoir longitudinal strain (LASr), and LA contraction longitudinal strain (LASct), respectively; $P_{Interaction}$ <0.001 for LA conduit longitudinal strain (LAScd)]. Univariate correlation analysis revealed that HT [LASr, r=–0.53, 95% confidence interval (CI): –0.62 to –0.42, P<0.001; LAScd, r=–0.49, 95% CI: –0.58 to –0.39, P<0.001; and LASct, r=–0.46, 95% CI: –0.55 to –0.34, P<0.001] and BMI categories (LASr, r=–0.68, 95% CI: –0.75 to –0.61, P<0.001; LAScd, r=–0.47, 95% CI: –0.57 to –0.35, P<0.001; and LASct, r=–0.73, 95% CI: –0.78 to –0.66, P<0.001) were negatively correlated with LA strains. A generalized linear model further demonstrated that there was an interaction effect between HT and obesity on LA strains after adjusting for confounding factors (Model 2: LASr, $\beta_{HT*Obesity}$ =–1.91, 95% CI: –3.48 to –0.35, P=0.01; LAScd, $\beta_{HT*Obesity}$ =–3.26, 95% CI: –4.83 to –1.70, P<0.001; LASct, $\beta_{HT*Overweight}$ =–1.97, 95% CI: –3.03 to –0.91, P<0.001; $\beta_{HT*Obesity}$ =–1.54, 95% CI: –2.67 to –0.41, P=0.007).

Conclusions: Both HT and increasing BMI category had an adverse effect on LA function. The coexistence of HT and obesity further impaired LA performance in an interaction manner. Weight loss is essential to reduce the incidence of adverse cardiovascular events in hypertensive patients.

Keywords: Hypertension; obesity; interaction effect; left atrial function; three-dimensional echocardiography

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Introduction

Hypertension (HT) and obesity are public health challenges threatening the well-being of the global population. They are associated with numerous co-morbidities, such as cardiovascular disease, chronic kidney disease, glucose metabolism disorder, dyslipidemia, and obstructive sleep apnea (1-3). The prevalence of HT and obesity has been increasing in recent decades (4,5). HT is frequently associated with excess weight or obesity. Both HT and obesity are risk factors for left atrial (LA) dilatation and dysfunction. Some previous studies have shown that patients with HT or obesity have LA dilatation and decreased LA phasic function, which are closely related to the occurrence of atrial fibrillation, heart failure, myocardial infarction, stroke and other adverse cardiovascular events (6-8). Therefore, it is of great significance for clinical management to explore the common influence of HT and obesity on LA function.

However, previous studies have considered HT and obesity as independent factors affecting LA function (9-11). Few studies have explored the simultaneous impact of HT and concomitant increasing body mass index (BMI) category on the changes in LA remodeling. The present study was conducted in order to compare LA phasic function in hypertensive patients and control participants with different BMI categories and to determine whether the negative effect of HT and increasing BMI category on LA function was independent or interactive.

The four-dimensional automated LA quantification (4D Auto LAQ) tool is a new software for analyzing LA structure and function, which is more accurate and sensitive than traditional two-dimensional echocardiography, because it can simultaneously obtain LA volume and strain parameters without geometric assumptions and angle dependence (12). We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1381/rc).

Methods

Study population

A total of 145 patients with essential HT treated at the Fuwai Central China Cardiovascular Hospital between September 2020 and November 2021 were prospectively enrolled in the study. HT was defined as blood pressure (BP) ≥140/90 mmHg or use of antihypertensive medications (13). Exclusion criteria were secondary or malignant HT, BMI <18.5 kg/m^2, age <18 years, left ventricular ejection fraction (LVEF) <50%, left ventricular (LV) outflow tract obstruction, overt coronary heart disease, atrial fibrillation or other serious arrhythmias, moderate or severe valvular stenosis or regurgitation, congenital heart disease, cardiomyopathy, malignant tumor, or other systemic diseases. One hundred and thirteen healthy volunteers who presented at the hospital for a physical examination during the same period were selected as the control group, and their BP, blood glucose, electrocardiogram, and echocardiogram results were normal. In the HT group, 8 patients with coronary artery disease, 2 patients with arrhythmia, 5 patients with valvular disease, 6 patients with diabetes, 4 patients with secondary HT, 3 patients with cardiomyopathy and 1 patient with congenital heart disease were excluded. In the control group, one subject each was excluded due to coronary artery disease, arrhythmia, and diabetes. Extremely obese patients with poor acoustic window were directly excluded in the process of image acquisition. One overweight hypertensive patient, 10 obese hypertensive patients, and 5 obese control participants were excluded during image analysis due to inadequate image quality. Hypertensive patients and control participants were both divided into three study subgroups according to the World Health Organization classifications as follows (14): normal weight (BMI 18.5–<25 kg/m^2), overweight (BMI 25–<30 kg/m^2), and obesity (BMI ≥30 kg/m^2) groups (*Figure 1*). This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of Fuwai Central China Cardiovascular Hospital (No. 202136). All subjects signed the informed consent form.

Image acquisition and measurements

The GE vivid E95 ultrasonic diagnostic instrument (GE Healthcare; Vingmed Ultrasound, Horten, Norway) with an M5S probe (frequency: 1.5–4.6 MHz) and a 4Vc probe (frequency: 1.4–5.2 MHz) were used for imaging. All participants underwent a complete transthoracic echocardiogram examination by the same experienced cardiac sonographer with the M5S probe. LV structure and function assessment was performed according to the guidelines of the American Society of Echocardiography (15). In the apical four-chamber view, transmitral early (E-wave) and late (A-wave) diastolic velocities were recorded using conventional pulsed-wave Doppler echocardiography at the mitral leaflet tips. The peak (e') of the mitral annular flow was recorded at both the septal and lateral annuli using

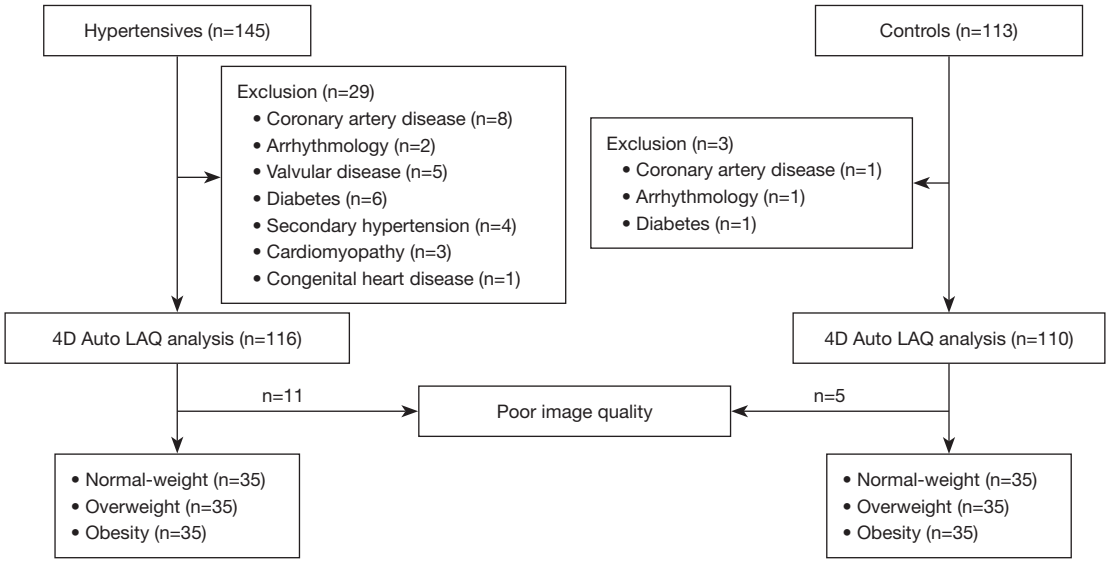

Figure 1 Flow chart for participant inclusion in the hypertensive and control groups. 4D Auto LAQ, four-dimensional automated left atrial quantification.

tissue Doppler. The average e' and average E/e' were then calculated. All participants also underwent an LA three-dimensional echocardiogram examination with a 4Vc probe. The electrocardiogram was connected synchronously during the collection process. The LA three-dimensional images were obtained for five consecutive cardiac cycles by adjusting the frame rate to 40% of the heart rate.

4D Auto LAQ analysis

All analyses were performed online using a dedicated 4D Auto LAQ software package and by two other experienced cardiac sonographers who had no knowledge of the subject's information. First, the operator selected Measure, Volume, and 4D Auto LAQ sub-mode sequentially for analysis. Then, the tracing point was dragged to the center of the mitral valve ring and the position and angle of the image were adjusted to make the vertical line intersect the center of the mitral valve and the vertex of the left atrium. After selecting review, the software automatically identified and wrapped the LA endocardium, and the operator manually adjusted the endocardium boundary until it was clear and intact. After choosing results, the system automatically obtained the LA volume and strain parameters (*Figure 2*). LA volume parameters included LA minimum volume (LAV_{min}), LA maximum volume (LAV_{max}), LA preatrial contraction volume (LAV_{preA}), and LA ejection fraction (LAEF). LA strain parameters included LA reservoir longitudinal strain (LASr), LA conduit longitudinal strain (LAScd), and LA contraction longitudinal strain (LASct). The LA wall lengthened during the reservoir phase, so the strain in this phase had a positive value. In the other two phases, the LA wall shortened, and the strains in these phases had negative values. All of the LA strain parameters were expressed as absolute values. The following equations were used for calculations:

- LA passive ejection fraction (LAPEF) = $(LAV_{max} - LAV_{preA})/LAV_{max} \times 100\%$;
- LA active ejection fraction (LAAEF) = $(LAV_{preA} - LAV_{min})/LAV_{preA} \times 100\%$;
- LA minimum volume index ($LAVI_{min}$) = $LAV_{min}/Height^2$;
- LA maximum volume index ($LAVI_{max}$) = $LAV_{max}/Height^2$;
- LA preatrial contraction volume index ($LAVI_{preA}$) = $LAV_{preA}/Height^2$;
- LV end-diastolic volume index (LVEDVI) = LV end-diastolic volume/$Height^2$;
- LV mass index (LVMI) = $0.8 \times 1.04 \times [(\text{inter-ventricular septum thickness} + \text{LV posterior wall thickness} + \text{LV end-diastolic diameter})^3 - \text{LV end-diastolic diameter}^3] + 0.6/Height^{2.7}$ (16).

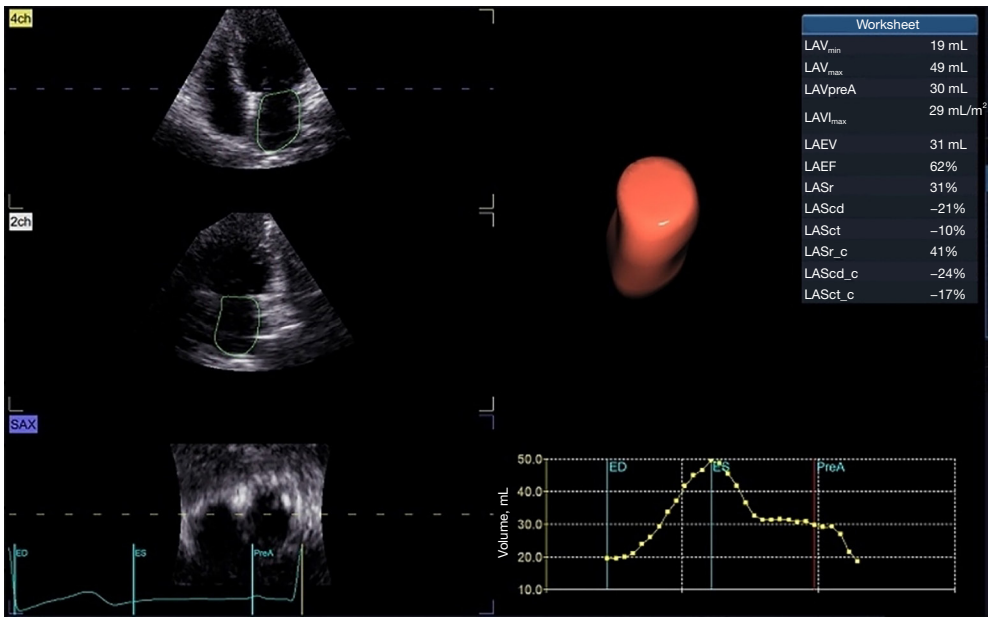

Figure 2 Quantitative analysis of the LA geometry and function using 4D Auto LAQ. ED, end-diastolic; ES, end-systolic; PreA, preatrial contraction; LA, left atrial; 4D Auto LAQ, four-dimensional automated left atrial quantification; LAV_{min}, left atrial minimum volume; LAV_{max}, left atrial maximum volume; LAVpreA, left atrial preatrial contraction volume; $LAVI_{max}$, left atrial maximum volume index; LAEV, left ventricular ejection volume; LAEF, left atrial ejection fraction; LASr, left atrial reservoir longitudinal strain; LAScd, left atrial conduit longitudinal strain; LASct, left atrial contraction longitudinal strain; LASr_c, left atrial reservoir circumferential strain; LAScd_c, left atrial conduit circumferential strain; LASct_c, left atrial contraction circumferential strain.

Sample size

The sample size was calculated using the PASS 15.0 (NCSS, LLC, Kaysville, UT, USA) software. Utilizing the factorial analysis of the variance program, the sample size was calculated using the results of the pre-experiment. The test level was set at α=0.05, the test efficiency was set at 1–β=0.85, and the sample size of each group was calculated to be at least 33 cases.

Statistical analysis

All data were analyzed using the SPSS 26.0 (IBM, Armonk, NY, USA) statistical software. Continuous variables were expressed as means ± standard deviations or medians [interquartile ranges (IQR)] according to the variable distribution. Categorical variables were represented as numbers (percentage). One-way analysis of variance was initially used to compare the continuous variables between groups. The χ^2 test was used to compare categorical variables, and Kruskal-Wallis test was used to compare non-normally distributed variables. Considering BP and BMI as the main factors within a 2×3 factorial design, general linear modeling analysis was used to explore the interaction effect between the two conditions on LA volumetric and functional parameters. Univariate correlations were used to explore the correlation between HT, BMI categories and LA strain. A generalized linear model was used to explore the associations between HT and BMI with LA strain indexes and to calculate the interaction term after adjustment for confounders. A first generalized linear model was built by adjusting for age and gender. A second generalized linear model was built by adjusting for heart rate, HT duration, smoking status, triglyceride (TG) level, high-density lipoprotein cholesterol (HDL-C) level, LVEF, LVMI, E/A, average e', average E/e', $LAVI_{min}$, $LAVI_{max}$, and $LAVI_{preA}$ on the basis of Model 1. Intra- and inter-observer variabilities of LA volumetric and functional parameters were assessed using the interclass correlation coefficients. A two-tailed P<0.05 was considered to indicate a statistically significant difference.

Results

Participant characteristics

Table 1 summarizes the main clinical, biochemical, medication use, and echocardiographic characteristics of the study groups categorized according to the BMI category. There were significant differences in body size, BP, TG, HDL-C, left atrial diameter (LAD), LVMI, and LV diastolic function between the six subgroups [P<0.001 for body surface area (BSA), BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), LAD, LVMI, E/A, average e', and average E/e'; P=0.004 for TG, P=0.01 for HDL-C, P=0.003 for LVEDVI]. There were no significant differences in other variables.

Three-dimensional echocardiography variables

Figure 3 shows that LA strain decreases with the increase of BMI grade. Furthermore, patients with HT had more impaired LA strain across all BMI categories compared to the controls. *Table 2* shows the main effects of BP and BMI on LA parameters, and their interaction effect on LA parameters. Specifically, these results demonstrate (I) the main effect of BP, with significant differences in LA volumetric and functional parameters between control and hypertensive patients, except for LAAEF (P_{BP} ≤0.001 for all); (II) the main effect of BMI, with significant differences in LA volumetric and functional parameters between groups categorized using BMI (P_{BMI} =0.04, 0.01, and 0.005 for $LAVI_{max}$, $LAVI_{preA}$, and LAPEF, respectively; P_{BMI} <0.001 for $LAVI_{min}$, LAEF, LAAEF, LASr, LAScd, and LASct); and (III) the interactive effect of BP and BMI, there was a significant interaction with LA functional parameters ($P_{Interaction}$ =0.04, 0.03, 0.005, 0.01, and 0.002 for LAEF, LAPEF, LAAEF, LASr, and LASct, respectively; $P_{Interaction}$ <0.001 for LAScd).

Association of BMI categories, HT, and LA strain

Table 3 shows univariate correlations of LA strain indexes for all study populations, and the results show that HT [LASr, r=–0.53, 95% confidence interval (CI): –0.62 to –0.42, P<0.001; LAScd, r=–0.49, 95% CI: –0.58 to –0.39, P<0.001; and LASct, r=–0.46, 95% CI: –0.55 to –0.34, P<0.001] and BMI categories (LASr, r=–0.68, 95% CI: –0.75 to –0.61, P<0.001; LAScd, r=–0.47, 95% CI: –0.57 to –0.35, P<0.001; and LASct, r=–0.73, 95% CI: –0.78 to –0.66, P<0.001) were negatively correlated with LA strains. *Table 4* shows a generalized linear model for LA strain indexes: (I) the main effect of BP, where the strain values of hypertensive patients were lower than those of the controls (Model 2: LASr, β_{HT} =–4.11, 95% CI: –5.39 to –2.83, P<0.001; LAScd, β_{HT} =–1.86, 95% CI: –3.14 to –0.58, P=0.004; LASct, β_{HT} =–2.01, 95% CI: –2.94 to –1.09, P<0.001); (II) the main effect of BMI, where the strain values of the overweight and obesity groups were lower than those of the normal-weight group (Model 2: LASr, $\beta_{Overweight}$ =–2.58, 95% CI: –3.64 to –1.52, P<0.001; $\beta_{Obesity}$ =–6.94, 95% CI: –8.16 to –5.72, P<0.001; LAScd, $\beta_{Overweight}$ =–1.40, 95% CI: –2.46 to –0.35, P=0.009; $\beta_{Obesity}$ =–2.80, 95% CI: –4.01 to –1.58, P<0.001; LASct, $\beta_{Overweight}$ =–1.30, 95% CI: –2.06 to –0.53, P=0.001; $\beta_{Obesity}$ =–4.88, 95% CI: –5.76 to –4.01, P<0.001); (III) the interactive effect of BP and BMI, where patients with HT and obesity had lower strain values than those without HT and with normal-weight. (Model 2: LASr, $\beta_{HT*Obesity}$ =–1.91, 95% CI: –3.48 to –0.35, P=0.01; LAScd, $\beta_{HT*Obesity}$ =–3.26, 95% CI: –4.83 to –1.70, P<0.001; LASct, $\beta_{HT*Overweight}$ =–1.97, 95% CI: –3.03 to –0.91, P<0.001; $\beta_{HT*Obesity}$ =–1.54, 95% CI: –2.67 to –0.41, P=0.007).

Reproducibility of LA parameter measurements

Intra- and inter-observer variabilities were measured in 20 randomly selected patients and the results showed excellent reproducibility (*Table 5*).

Discussion

The present study examined the LA function using three-dimensional echocardiography in hypertensive patients and control participants with different BMI categories. Our findings suggested that there was a significant interaction effect between HT and obesity on LA phasic function. The relationship between HT and obesity is dynamic, both of them contributing to LA remodeling. Hypertensive patients had a more impaired LA function in all categories of BMI compared to the controls, and the LA function of hypertensive patients was progressively impaired with the increasing BMI category.

Arterial HT is one of the main causes of cardiac damage, which leads to LA morphological and functional changes (17). LA dilatation is an early event in patients with arterial HT, which is present in about 30% of hypertensive patients (18,19). LA dysfunction in hypertensive patients is closely related to LV pressure overload. Long-term increased arterial pressure leads to hypertrophy and fibrosis of LV cardiomyocytes, which then leads to LV diastolic

Table 1 General characteristics of patients in all study groups

Variables	Controls (n=105)			Hypertensives (n=105)			P value
	Normal-weight (n=35)	Overweight (n=35)	Obesity (n=35)	Normal-weight (n=35)	Overweight (n=35)	Obesity (n=35)	
Clinical							
Age (years)	43.91±9.98	44.88±10.78	47.68±11.42	47.82±7.81	46.14±10.06	43.31±9.77	0.22
Male	16 (45.7)	19 (54.3)	23 (65.7)	16 (45.7)	20 (57.1)	22 (62.9)	0.41
BSA (m^2)	1.71±0.15	1.81±0.15	2.00±0.13	1.72±0.14	1.89±0.12	1.99±0.14	<0.001
BMI (kg/m^2)	23.00±1.75	26.09±0.95	31.01±0.87	23.53±1.47	27.59±1.20	31.44±1.68	<0.001
Heart rate (bpm)	68.02±6.83	71.74±9.38	68.40±8.45	70.91±7.74	72.54±8.71	69.31±10.46	0.16
HT duration (years)	–	–	–	3.00 [1.00, 6.00]	3.00 [1.00, 6.00]	3.00 [1.00, 7.00]	0.82
SBP (mmHg)	123.05±8.45	122.88±8.90	124.45±8.57	152.17±8.64	154.48±10.50	159.65±17.53	<0.001
DBP (mmHg)	79.45±6.36	79.37±6.61	80.88±6.01	102.20±11.41	96.97±9.02	103.40±15.50	<0.001
Current smokers	9 (25.7)	11 (31.4)	10 (28.6)	7 (20.0)	12 (34.3)	16 (45.7)	0.28
Biochemical							
HbA1c (%)	5.20±0.28	5.24±0.35	5.26±0.28	5.48±0.74	5.55±0.86	5.26±0.77	0.08
TC (mmol/L)	3.97±0.85	4.11±1.01	3.88±0.95	4.23±1.05	4.24±0.88	4.23±0.79	0.45
TG (mmol/L)	1.32±0.48	1.35±0.62	1.58±1.08	1.56±0.92	1.95±1.16	2.10±1.39	0.004
HDL-C (mmol/L)	1.27±0.27	1.23±0.25	1.16±0.31	1.18±0.29	1.10±0.28	1.05±0.27	0.01
LDL-C (mmol/L)	2.56±0.88	2.52±0.99	2.16±0.81	2.71±0.86	2.69±0.83	2.63±0.69	0.09
eGFR (mL/min/1.732 m^2)	101.47±9.77	101.39±8.94	99.48±9.35	102.29±11.37	97.43±11.35	101.72±15.56	0.47
Medication use							
Beta-blockers	–	–	–	5 (14.3)	6 (17.1)	8 (22.9)	0.64
CCBs	–	–	–	21 (60.0)	16 (45.7)	19 (54.3)	0.48
ACEIs/ARBs	–	–	–	19 (54.3)	12 (34.3)	17 (48.6)	0.22
Diuretics	–	–	–	6 (17.1)	4 (11.4)	5 (14.3)	0.79
Statins	–	–	–	8 (22.9)	5 (14.3)	7 (20.0)	0.65
Aspirin	–	–	–	1 (2.9)	2 (5.7)	2 (5.7)	0.81
Echocardiography							
LAD (mm)	30.68±2.75	31.34±2.48	31.97±2.78	33.25±2.94	35.57±3.47	38.05±4.44	<0.001
LVEDVI (mL/m^2)	33.93±5.70	35.03±5.31	34.78±6.85	34.29±6.76	35.16±5.92	39.50±6.59	0.003
LVEF (%)	63.71±3.08	63.82±3.23	63.57±2.87	64.74±2.90	63.74±2.41	63.65±4.00	0.64
LVMI ($g/m^{2.7}$)	34.82±6.05	36.12±6.40	35.46±5.71	40.52±8.97	43.99±7.65	48.04±12.57	<0.001
E/A	1.44±0.32	1.41±0.41	1.43±0.31	1.11±0.20	1.02±0.23	1.07±0.32	<0.001
Average e' (m/s)	0.14±0.02	0.12±0.03	0.12±0.02	0.10±0.02	0.09±0.02	0.10±0.02	<0.001
Average E/e'	6.21±1.27	6.79±1.69	7.29±2.15	8.21±1.91	8.26±1.87	8.22±2.43	<0.001

Data are presented as mean ± standard deviation if in normal distribution or as median [interquartile ranges] if not in normal distribution. Categorical variables are presented as numbers (percentage). P value, total P value between groups; BSA, body surface area; BMI, body mass index; HT, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; CCBs, calcium channel blockers; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; LAD, left atrial diameter; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; E/A, ratio of early peak diastolic velocity to late peak diastolic velocity of mitral valve orifice; average e', the average of peak e' of mitral annular flow recorded at the septal and lateral annulus; average E/e', ratio of E to average e'.

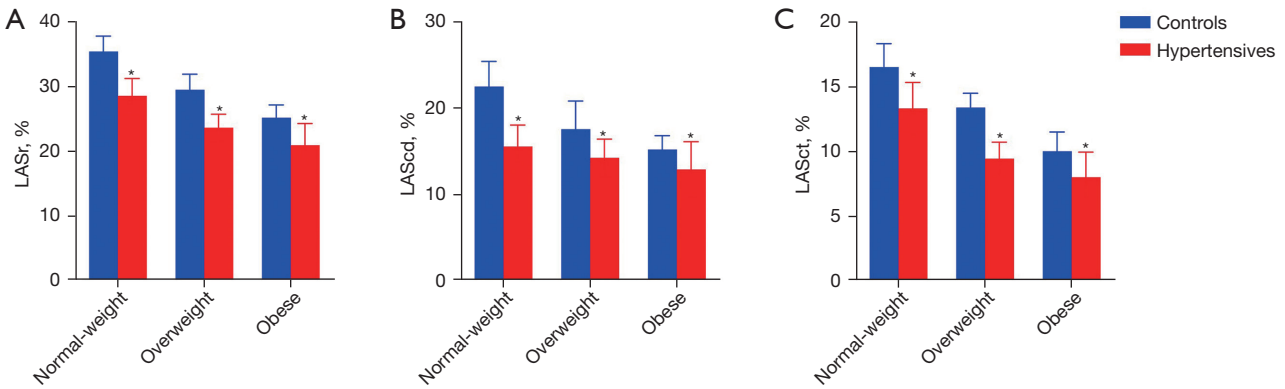

Figure 3 Comparisons of LA strain between hypertensive patients and control participants within the same BMI categories. Comparisons of LASr (A), LAScd (B), and LASct (C) between hypertensive patients and control participants in the same BMI categories. *, P<0.05 for hypertensives *vs.* controls in the same BMI categories. LA, left atrial; BMI, body mass index; LASr, left atrial reservoir longitudinal strain; LAScd, left atrial conduit longitudinal strain; LASct, left atrial contraction longitudinal strain.

Table 2 Three-dimensional echocardiographic characteristics of patients in all study groups

Variables	Controls (n=105)			Hypertensives (n=105)			BP		BMI		Interaction	
	Normal-weight (n=35)	Overweight (n=35)	Obesity (n=35)	Normal-weight (n=35)	Overweight (n=35)	Obesity (n=35)	F_{BP}	P_{BP}	F_{BMI}	P_{BMI}	$F_{Interaction}$	$P_{Interaction}$
$LAVI_{min}$ (mL/m^2)	6.05±1.37	6.24±1.06	7.58±1.94	7.24±1.78	7.94±2.37	9.18±4.34	20.39	<0.001	9.92	<0.001†‡	0.21	0.80
$LAVI_{max}$ (mL/m^2)	16.09±3.30	15.89±2.57	17.48±4.08	18.20±3.50	18.16±5.10	20.13±7.95	12.71	<0.001	3.07	0.04†‡	0.05	0.94
$LAVI_{preA}$ (mL/m^2)	9.84±2.26	10.39±1.90	11.82±2.78	12.63±2.89	12.69±3.57	14.14±6.24	25.08	<0.001	4.73	0.01†‡	0.10	0.90
LAEF (%)	62.77±3.15	60.48±4.67	56.77±4.54	60.31±4.94	56.17±5.58	54.97±7.18	11.98	0.001	18.20	<0.001*†‡	3.21	0.04
LAPEF (%)	38.81±5.59	34.61±6.21	32.30±6.26	30.85±6.69	29.87±5.96	30.30±8.41	29.06	<0.001	5.39	0.005*†	3.61	0.03
LAAEF (%)	38.23±6.38	39.49±5.28	35.74±5.19	42.72±5.18	37.60±5.98	35.24±7.49	0.72	0.40	12.37	<0.001†‡	5.51	0.005
LASr (%)	35.31±2.38	29.42±2.40	25.11±1.98	28.48±2.68	23.57±2.09	20.88±3.35	261.78	<0.001	220.74	<0.001*†‡	4.74	0.01
LAScd (%)	22.45±2.89	17.51±3.24	15.17±1.59	15.51±2.48	14.22±2.14	12.85±3.20	123.96	<0.001	56.64	<0.001*†‡	14.69	<0.001
LASct (%)	16.45±1.80	13.34±1.10	9.97±1.48	13.28±2.00	9.40±1.28	7.97±1.94	179.72	<0.001	228.54	<0.001*†‡	6.21	0.002

Data are presented as mean ± standard deviation. *, P_{BMI} <0.05 for overweight group *vs.* normal-weight group; †, P_{BMI} <0.05 for obesity group *vs.* normal-weight group; ‡, P_{BMI} <0.05 for obesity group *vs.* overweight group. BP, blood pressure; BMI, body mass index; $LAVI_{min}$, left atrial minimum volume index; $LAVI_{max}$, left atrial maximum volume index; $LAVI_{preA}$, left atrial preatrial contraction volume index; LAEF, left atrial ejection fraction; LAPEF, left atrial passive ejection fraction; LAAEF, left atrial active ejection fraction; LASr, left atrial reservoir longitudinal strain; LAScd, left atrial conduit longitudinal strain; LASct, left atrial contraction longitudinal strain; F_{BP}, F value when BP as the main effect; F_{BMI}, F value when BMI as the main effect.

dysfunction and increased filling pressure (20,21). Due to the thinner wall and shorter myocardial fibers compared to the left ventricle, the left atrium is intolerant to both pressure and volume load, resulting in reduced LA compliance and deformability (22). Previous studies have shown the adverse effects of HT on LA function (23,24). The results of this study also showed that the LA phasic volume increased and the LA phasic function decreased in the hypertensive group.

Obesity increases stroke volume, cardiac output and

Table 3 Univariate correlations of LA strain indexes

Variable	LASr		LAScd		LASct	
	r	P value	r	P value	r	P value
Age (years)	–0.11	0.09	–0.19	0.005	0.05	0.43
Sex, male	–0.24	0.001	–0.18	0.008	–0.16	0.02
BMI categories	–0.68	<0.001	–0.47	<0.001	–0.73	<0.001
HT	–0.53	<0.001	–0.49	<0.001	–0.46	<0.001
HT duration (years)	–0.29	<0.001	–0.29	<0.001	–0.24	0.001
Current smokers	–0.19	0.004	–0.14	0.04	–0.14	0.04
TG (mmol/L)	–0.19	0.005	–0.14	0.04	–0.22	0.001
HDL-C (mmol/L)	0.18	0.007	0.15	0.03	0.19	0.005
LVEF (%)	0.03	0.65	–0.01	0.86	0.08	0.22
LVMI ($g/m^{2.7}$)	–0.40	<0.001	–0.40	<0.001	–0.29	<0.001
E/A	0.33	<0.001	0.39	<0.001	0.22	0.002
Average e' (m/s)	0.48	<0.001	0.49	<0.001	0.35	<0.001
Average E/e'	–0.33	<0.001	–0.34	<0.001	–0.26	<0.001

LA, left atrial; BMI, body mass index; HT, hypertension; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; E/A, ratio of early peak diastolic velocity to late peak diastolic velocity of mitral valve orifice; average e', the average of peak e' of mitral annular flow recorded at the septal and lateral annulus; average E/e', ratio of E to average e'; LASr, left atrial reservoir longitudinal strain; LAScd, left atrial conduit longitudinal strain; LASct, left atrial contraction longitudinal strain.

circulating blood volume, while reducing peripheral vascular resistance, which leads to LV dilation, eccentric hypertrophy, and diastolic dysfunction (25). There is evidence that obesity-related insulin resistance, inflammatory process, and subsequent neurohormonal activation increase oxidative stress and adipokine concentrations, promoting infiltration of free fatty acids in vascular walls and cardiomyocytes, which leads to atherosclerosis, myocardial hypertrophy, and increased interstitial fibrosis (26-28). Previous studies have shown that obesity or increased BMI is independently associated with cardiac systolic and diastolic dysfunction, LA enlargement, and LA dysfunction (29,30). Deal *et al.* have found that LA dysfunction was present in obese individuals even in the absence of cardiovascular risk factors such as HT (31). Abed *et al.* have found that LA size, histology, conduction, and expression of profibrotic mediators changed with progressive obesity, leading to LA dysfunction (32). The results of the present study also indicated that obesity was closely related to LA dysfunction.

There is strong evidence that increased BMI is a principal risk factor for HT since the prevalence of HT increases sharply with increasing body weight (33,34). Although HT and obesity frequently coexist, previous studies have considered HT and obesity as independent factors affecting heart function. Few studies have assessed the combined impact of both HT and obesity on LA function. Tadic *et al.* have demonstrated that obesity significantly impacted BP variability and LA phasic function in untreated hypertensive patients, while LA reservoir and conduit function were gradually reduced in increasingly obese individuals (35). Miyoshi *et al.* have demonstrated a synergistic effect of obesity on LA dysfunction in hypertensive patients (36,37). Parati *et al.* have shown that increased sympathetic drive, inhibition of arterial and cardiopulmonary reflex, reduced physical activity, and sleep disturbance are additional mechanisms for LA remodeling in overweight and obese hypertensive patients (38). Although the underlying pathogenesis of hypertensive and obese cardiomyopathy may be different and multipathway, ultimately the common

Table 4 Generalized linear model

Variable	Unadjusted*		Model 1†		Model 2‡	
	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value
LASr						
Overweight	−2.68 (−3.85 to −1.52)	<0.001	−2.82 (−3.95 to −1.69)	<0.001	−2.58 (−3.64 to −1.52)	<0.001
Obesity	−7.60 (−8.76 to −6.43)	<0.001	−7.66 (−8.82 to −6.50)	<0.001	−6.94 (−8.16 to −5.72)	<0.001
HT	−4.22 (−5.39 to −3.06)	<0.001	−4.39 (−5.53 to −3.25)	<0.001	−4.11 (−5.39 to −2.83)	<0.001
HT*Overweight	−1.62 (−3.27 to 0.02)	0.05	−1.24 (−2.84 to 0.35)	0.12	−1.07 (−2.54 to 0.39)	0.15
HT*Obesity	−2.60 (−4.24 to −0.95)	0.002	−2.17 (−3.79 to −0.56)	0.008	−1.91 (−3.48 to −0.35)	0.01
LAScd						
Overweight	−1.37 (−2.60 to −0.14)	0.02	−1.54 (−2.73 to −0.35)	0.01	−1.40 (−2.46 to −0.35)	0.009
Obesity	−2.65 (−3.88 to −1.42)	<0.001	−2.85 (−4.07 to −1.63)	<0.001	−2.80 (−4.01 to −1.58)	<0.001
HT	−2.31 (−3.54 to −1.08)	<0.001	−2.55 (−3.75 to −1.34)	<0.001	−1.86 (−3.14 to −0.58)	0.004
HT*Overweight	−0.97 (−2.71 to 0.76)	0.27	−0.57 (−2.26 to 1.12)	0.51	−0.55 (−2.20 to −0.91)	0.46
HT*Obesity	−4.62 (−6.36 to −2.88)	<0.001	−4.10 (−5.81 to −2.39)	<0.001	−3.26 (−4.83 to −1.70)	<0.001
LASct						
Overweight	−1.42 (−2.18 to −0.67)	<0.001	−1.37 (−2.12 to −0.62)	<0.001	−1.30 (−2.06 to −0.53)	0.001
Obesity	−5.31 (−6.07 to −4.55)	<0.001	−5.26 (−6.03 to −4.49)	<0.001	−4.88 (−5.76 to −4.01)	<0.001
HT	−2.00 (−2.75 to −1.24)	<0.001	−1.93 (−2.68 to −1.17)	<0.001	−2.01 (−2.94 to −1.09)	<0.001
HT*Overweight	−1.94 (−3.01 to −0.87)	<0.001	−2.07 (−3.14 to −1.00)	<0.001	−1.97 (−3.03 to −0.91)	<0.001
HT*Obesity	−1.17 (−2.24 to −0.09)	0.03	−1.33 (−2.41 to −0.25)	0.01	−1.54 (−2.67 to −0.41)	0.007

Unadjusted*: including BMI categories and hypertension. Model 1†: adjusted for age and sex. Model 2‡: adjusted as Model 1, plus heart rate, hypertension duration, smoking status, TG, HDL-C, LVEF, LVMI, E/A, average e', average E/e', $LAVI_{min}$, $LAVI_{max}$, and $LAVI_{preA}$. HT*Overweight, patients with hypertension and overweight; HT*Obesity, patients with hypertension and obesity. HT, hypertension; LASr, left atrial reservoir longitudinal strain; LAScd, left atrial conduit longitudinal strain; LASct, left atrial contraction longitudinal strain; CI, confidence interval; BMI, body mass index; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; E/A, ratio of early peak diastolic velocity to late peak diastolic velocity of mitral valve orifice; average e', the average of peak e' of mitral annular flow recorded at the septal and lateral annulus; average E/e', ratio of E to average e'; $LAVI_{min}$, left atrial minimum volume index; $LAVI_{max}$, left atrial maximum volume index; $LAVI_{preA}$, left atrial preatrial contraction volume index.

pathway is increased myocardial fibrosis, which eventually leads to myocardial dysfunction (39-41).

The present single-center study had no follow-up clinical outcome data, so the development and transformation of LA function in hypertensive patients with different BMI levels could not be observed. The study subjects will be followed up in order to observe the changes in LA function as BMI changes. In addition, since most of the hypertensive patients included in the study were taking antihypertensive drugs, the effect of drugs on myocardial function was not considered.

Conclusions

The present study showed a significant interaction effect between HT and obesity on LA phasic function in hypertensive patients. Therefore, when there are risk factors such as HT and obesity, we should pay more attention to the LA structure and function, so as to conduct early intervention and treatment for patients and avoid adverse outcomes as far as possible. Controlling HT to a stable level is of the essence for reducing cardiac morbidity and weight loss is also of great significance in reducing cardiac

Table 5 Intra- and Inter-observer variability of the 4D Auto LAQ parameters

Variable	Intra-observer reproducibility		Inter-observer reproducibility	
	ICC	95% CI	ICC	95% CI
LAV_{min}	0.994	0.981–0.998	0.998	0.994–0.999
LAV_{max}	0.997	0.991–0.999	0.998	0.993–0.999
LAV_{preA}	0.990	0.967–0.997	0.996	0.985–0.999
LAEF	0.995	0.984–0.999	0.993	0.976–0.998
LASr	0.975	0.915–0.993	0.987	0.957–0.996
LAScd	0.966	0.882–0.990	0.926	0.744–0.979
LASct	0.967	0.890–0.990	0.935	0.772–0.981

LAV_{min}, left atrial minimum volume; LAV_{max}, left atrial maximum volume; LAV_{preA}, left atrial preatrial contraction volume; LAEF, left atrial ejection fraction; LASr, left atrial reservoir longitudinal strain; LAScd, left atrial conduit longitudinal strain; LASct, left atrial contraction longitudinal strain; 4D Auto LAQ, four-dimensional automated left atrial quantification; ICC, intra-class correlation coefficient; CI, confidence interval.

morbidity and mortality in hypertensive patients.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was reviewed and approved by the Ethics Committee of Fuwai Central China Cardiovascular Hospital (No. 202136). The participants provided their written informed consent to participate in this study.

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