ORIGINAL RESEARCH ARTICLE

The patterns of left ventricular alteration by adipose tissue distribution: implication for heart failure prevention

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Abstract

Aims The current study aimed to evaluate the associations between general and abdominal obesity with left ventricular (LV) structure and function and whether these associations differed by sex.

Methods and results This is a community-based cross-sectional study, and 971 hypertensive individuals without overt cardiovascular disease were included. General obesity was defined as body mass index (BMI) $\geq$ 28 kg/m^2, and abdominal obesity was defined as waist circumference (WC) $\geq$ 90 cm for men and $\geq$85 cm for women. The associations between general and abdominal obesity with LV structure and function were examined using linear regression analysis, and the interaction by sex was performed. The mean age was 66.5 ± 11.4 years, and women accounted for 62%. General obese individuals (*n* = 205) were more likely to have concentric remodelling, LV hypertrophy, and worse diastolic function. Similar differences were observed in abdominal obese individuals (*n* = 593). General obesity was associated with LV end-diastolic volume, LV mass, left atrial volume, and septal E/e' ratio after adjusting for WC and clinical covariates; and abdominal obesity was associated with septal e' velocity after adjusting for BMI and clinical covariates. The associations between general obesity with LV structure and function did not differ by sex, while the magnitudes of the associations between abdominal obesity with LV mass and septal e' velocity were greater in men.

Conclusions General and abdominal obesity were associated with different patterns of LV structural and functional alterations, stressing the importance of incorporating BMI and WC measurements into assessing obesity-related LV alterations.

Introduction

Obesity prevalence has grown rapidly in China and worldwide.[1–5] Results from the 2013–2014 National Chronic Disease and Risk Factor Surveillance have shown that the prevalence of general obesity, which is defined as body mass index (BMI) $\geq$ 28 kg/m^2, in Chinese adults was 14.0% and the prevalence of abdominal obesity, which is defined as waist circumference (WC) $\geq$ 90 cm for men and $\geq$85 cm for women, was 31.5%.[1] Obesity is associated with left ventricular hypertrophy (LVH) and diastolic dysfunction,[6–11] which predispose to heart failure with preserved ejection fraction (HFpEF).

Studies have assessed and compared the pattern of left ventricular (LV) structural and functional alterations in association with different forms of adipose tissue distribution (e.g. general vs. abdominal), and the results are mixed.[6,7,10–13] Further investigation is needed as better understanding the obesity-related LV alterations would help guide management in the future.

Although studies of western populations have demonstrated the association between obesity and LV structural and functional alterations,[6–11] the evidence is notably lacking in the Chinese community populations. In addition, prior studies demonstrate that there are differences in body

composition across ethnic groups,[14–20] as its impacts on cardiac remodelling. For example, the US cohort study suggests that the increase in the mean LV mass (LVM) with per 10 kg increase in fat mass was higher in American Chinese men than Caucasian men,[7] and the cut-off value of LVM index to predict cardiovascular events was lower in Chinese than that in Caucasians.[21] Ethnic-specific normative references for indices of LV structure and function have also been proposed.[22] These findings together demonstrate the need and importance to assess the relationship between obesity and LV structural and functional alterations in the Chinese community populations.

Accordingly, leveraging data from the community hypertensive individuals without overt cardiovascular disease, the aims of the current study were to cross-sectionally assess the associations between general and abdominal obesity with LV structural and functional alterations, respectively. Considering the higher prevalence of HFpEF among women than men,[23–25] we further evaluated whether obesity rendered greater influences on LV structure and function among women.

Methods

Study participants

This is a community-based cross-sectional study. Participants were enrolled from the Liaobu County, Dongguan, Guangdong Province, during the government-sponsored annual health examination. The current study was approved by the Clinical Research Ethics Committee of Guangdong Provincial People's Hospital and the Liaobu County Health Department. Written informed consent was obtained before enrolment. The definition of hypertension was based on prior physician's diagnosis and/or use of antihypertensive drug. A total of 1474 hypertensive individuals underwent echocardiographic examination during annual health examination in 2016, and individuals who did not have tissue Doppler imaging data ($n = 464$) and who had prior ischaemic stroke ($n = 23$) or coronary heart disease ($n = 24$) were excluded, and 971 hypertensive individuals without overt cardiovascular disease were included in the current analyses (*Figure 1*).

Clinical characteristics and laboratory analyses

Participants underwent baseline evaluation by trained healthcare staffs during the annual health examination. Standardized questionnaire forms were used to collect information about age, sex, smoking status, physical activity, prior medical history, and current medication use. Fasting venous blood was used for the evaluation of fasting plasma glucose, lipid profiles, and serum levels of uric acid and creatinine, which was then used to calculate the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease formula,[26] and an eGFR < 60 mL/min/1.73 m^2 was defined as chronic kidney disease. Hyperuricaemia was defined as serum uric acid ≥ 420 μmol/L for men and ≥ 360 μmol/L for women, respectively.[27]

Figure 1 Study flow chart.
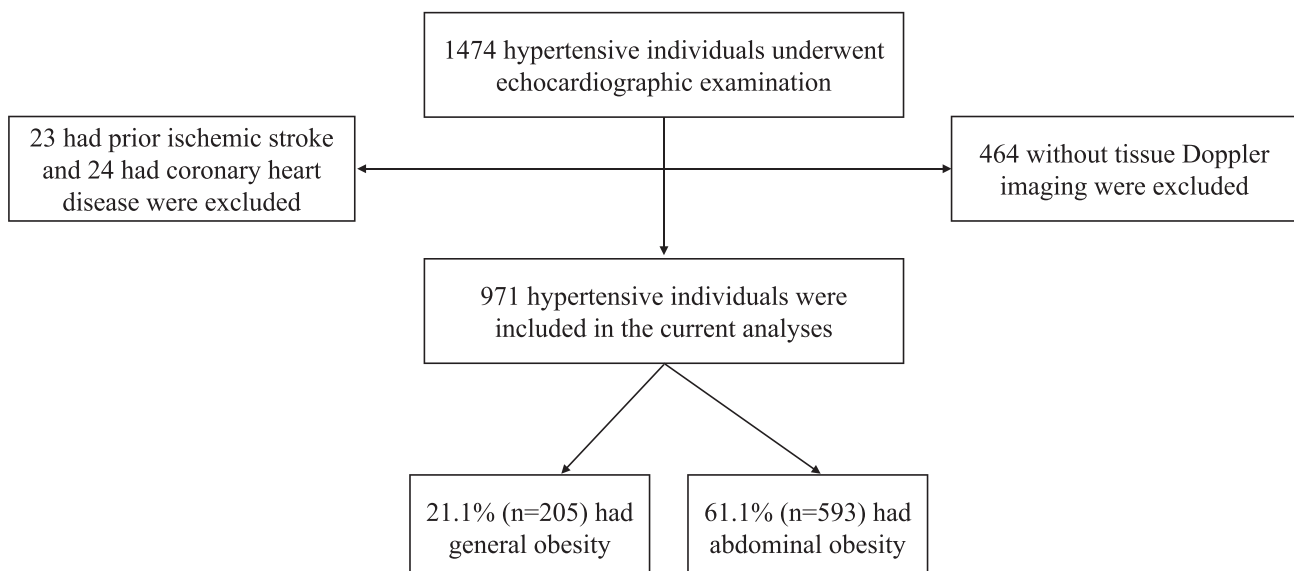
Blood pressure and anthropometric measurements

Prior to blood pressure (BP) measurements, participants were required to stay at rest in a sitting position for 5 min. According to the Chinese hypertension guideline,[28] two BP measurements were performed with at least 1 min interval with upper arm kept at the heart level using the Omron HEM-7051 device (Omron HealthCare, Kyoto, Japan). The average value of two BP readings was recorded. If the first two BP readings differed by >5 mmHg, an additional BP measurement was performed, and the mean value of three readings was recorded. Pulse pressure was calculated as systolic BP minus diastolic BP.

Weight and height were measured with participants standing without wearing heavy clothes or shoes by trained healthcare staffs. Body weight was determined using an electronic scale, and height was measured with a wall-mounted stadiometer. BMI was calculated by weight in kilograms divided by height in squared metres, with a value ≥ 28 kg/m^2 was defined as general obesity.[29] WC was measured at the level of the midpoint between the top of the iliac crest and the lower margin of the last palpable rib in the midaxillary line, with a value ≥ 90 cm for men and ≥ 85 cm for women was defined as abdominal obesity.[1] Body surface area (BSA) was calculated as follows: BSA (m^2) = (Weight [kg]$^{0.425}$ * Height [cm]$^{0.725}$) * 0.007184.

Echocardiographic examination

Transthoracic echocardiography was performed using a Vivid S6 M4S-RS Probe (GE Ving-Med) interfaced with a 2.5 to 3.5 MHz phased-array probe by a trained cardiologist (D. Z.). All the examinations were performed according to the American Society of Echocardiography guideline recommendation.[30] The left atrial (LA) volume was assessed using the modified biplane Simpson's rule from the apical two-chamber and four-chamber views at end systole. LA volume was indexed to BSA, with a value >34 mL/m^2 was considered LA enlargement.[31] The LV linear dimensions were measured from a parasternal long-axis view. Relative wall thickness was calculated as (septal wall thickness + LV posterior wall thickness) divided by LV end-diastolic diameter, and relative wall thickness > 0.42 was considered concentric remodelling. LV end-diastolic diameter, LV posterior wall thickness, and septal wall thickness at diastole were used to calculate LVM. LVM was indexed to BSA, with a value ≥ 115 g/m^2 for men and ≥ 95 g/m^2 for women was considered LVH. Based on the presence of concentric remodelling and LVH, LV geometry was classified into normal, concentric remodelling, and concentric and eccentric hypertrophy. Stroke volume (SV) was calculated as LV end-diastolic volume (LVEDV) minus LV end-systolic volume. The LV ejection fraction (LVEF) was calculated based on modified biplane Simpson's rule. Mitral inflow velocity (peak E-wave and A-wave) was assessed using pulsed-wave Doppler from the apical four-chamber view. Peak early systolic tissue velocity (S') and peak early diastolic tissue velocity (e') were measured from the septal aspect of the mitral annulus. According to the guideline recommendation,[31] septal e' velocity < 7 cm/s was considered LV diastolic dysfunction and septal E/e' ratio > 15 was considered an increased LV filling pressure.

Statistical analysis

Continuous variables were presented as mean ± standard deviation if normal distribution, otherwise were presented as median and interquartile range. Categorical variables were presented as number and proportion. Differences in clinical characteristics, laboratory measurements, BP value, and indices of LV structure and function were tested between (i) general obesity vs. non-general obesity and (ii) abdominal obesity vs. non-abdominal obesity using Student's t-test or Mann–Whitney U test for continuous variables and χ^2 test or Fisher's exact test for categorical variables. To evaluate the trend in LV structural and functional alterations with increasing BMI and WC, participants were separated into four groups according to the sex-specific quartiles of BMI and WC, respectively, and a P-value for trend was reported. The correlation between BMI and WC with metabolic variables [fasting plasma glucose, triglyceride, and high-density lipoprotein cholesterol (HDL-C)] and systolic and diastolic BP was determined using Pearson correlation coefficients. The association between general and abdominal obesity with indices of LV structure and function was assessed using linear regression analyses with adjusting for covariates (age, sex, smoking status, physical activity, systolic BP, dyslipidaemia, diabetes mellitus, eGFR, uric acid, antihypertensive drugs, BMI, and WC). Unstandardized coefficient (β) and associated 95% confidence interval were reported. As a sensitivity analysis, general and abdominal obesity were substituted by BMI and WC, respectively, in the linear regression model, and results were reported in the Supporting Information, *Table S1*. We further examined whether sex modified the relationship between general and abdominal obesity with indices of LV structure and function with adjusting for covariates as described earlier. Unstandardized β (95% confidence interval) and a P-value for interaction were reported. All the analyses were performed using the R package (Version 3.6, Vienna), and a P-value < 0.05 was considered as statistical significance.

Results

Among the 971 community hypertensive individuals, 205 were general obesity (21.1%) and 593 were abdominal obesity (61.1%). The mean BMI and WC were 25.3 ± 3.8 kg/m^2 and 90.0 ± 9.4 cm, respectively. The mean age was 66.5 ± 11.4 years, and women accounted for 62% (*n* = 602) of the current study. The mean systolic BP and diastolic BP were 137.0 ± 16.7 mmHg and 81.9 ± 10.5 mmHg, respectively.

Baseline characteristic comparisons according to general and abdominal obesity

As shown in *Table 1*, individuals with general obesity were younger; were more likely to be women; were less likely to smoke; had a higher WC, fasting plasma glucose, triglyceride, and HDL-C; were more likely to have dyslipidaemia, diabetes mellitus, and hyperuricaemia; and had a higher proportion on statins and antidiabetics.

Individuals with abdominal obesity were more likely to be women; were less likely to smoke; had a higher BMI, fasting plasma glucose, triglyceride, and HDL-C; were more likely to have dyslipidaemia, diabetes mellitus, and hyperuricaemia; and had a higher proportion on antidiabetics, angiotensin receptor blocker, and calcium channel blocker.

Left ventricular structure and function comparisons according to general and abdominal obesity

Individuals with general obesity had a larger LVEDV and SV, a higher LVM and LV mass-to-volume (LVMV) ratio, and a higher prevalence of LVH (*Table 2*). There was no difference in LVEF and septal S' velocity. Individuals with general obesity had a larger LA volume and a higher septal E/e' ratio. These differences were also observed between individuals with and without abdominal obesity. In addition, individuals with abdominal obesity had a lower septal e' velocity.

Trend in left ventricular structural and functional alterations with increasing body mass index and waist circumference

There was a trend in increasing LVEDV, SV, LVM, LVMV ratio, LA volume, and septal E/e' ratio with increasing BMI and WC, respectively (*Figure 2*). In addition, there was a trend in decreasing septal e' velocity with increasing WC.

Correlation between body mass index and waist circumference with metabolic factors and blood pressure

Both BMI and WC were positively correlated to serum levels of fasting plasma glucose, triglyceride, and diastolic BP, while negatively correlated to HDL-C (*Figure 3*).

Association of general and abdominal obesity with indices of left ventricular structure and function

Both general and abdominal obesity were associated with LVEDV, SV, LVM, LVMV ratio, LA volume, septal E/e' ratio, and septal e' velocity after adjusting for clinical covariates (*Table 3*). General obesity remained associated with LVEDV, LVM, LA volume, and septal E/e' ratio after further adjusting for WC, and abdominal obesity remained associated with septal e' velocity after further adjusting for BMI. In the sensitivity analysis (Supporting Information, *Table S1*), after adjusting for clinical covariates and WC, BMI remained associated with LVEDV, SV, LVM, LVMV ratio, LA volume, and septal E/e' ratio, while after adjusting for clinical covariates and BMI, WC remained associated with LVEDV and septal e' velocity.

In the interaction analysis, after adjusting for covariates, the associations between general obesity with indices of LV structure and function were not modified by sex (*Table 4*), while the magnitudes of the associations between abdominal obesity with LVM and septal e' velocity were greater in men and in women.

Discussion

There are some important findings of the current study. Among community hypertensive individuals without overt cardiovascular disease, compared with non-obese individuals, those with obese, both general and abdominal, had worse alterations of LV structure and function. There were some differences in the pattern of general and abdominal obesity-related LV alterations. Specifically, general obesity was associated with increased LVEDV, LVM, and LV filling pressure (indexed by LA volume and septal E/e' ratio), while abdominal obesity was only associated with impaired LV relaxation (indexed by septal e' velocity). The influences of general obesity on LV structural and functional alterations were consistent in men and women, while abdominal obesity appeared to have greater influences on LVM and septal e' velocity in men than in women. These findings together suggest that general and abdominal obesity might play somewhat differential roles in LV structural and functional alterations,

Table 1 Baseline characteristic comparisons according to general and abdominal obesity

Variables	General obesity (n = 205)	Non-general obesity (n = 766)	P-value	Abdominal obesity (n = 593)	Non-abdominal obesity (n = 378)	P-value
Age (years)	64.0 ± 12.1	67.1 ± 11.2	<0.001	66.0 ± 11.2	67.2 ± 11.8	0.10
Women, n (%)	144 (70.2)	458 (59.8)	0.01	405 (68.3)	197 (52.1)	<0.001
Systolic BP (mmHg)	136.7 ± 16.1	137.1 ± 16.8	0.75	137.3 ± 16.2	136.6 ± 17.3	0.56
Diastolic BP (mmHg)	82.6 ± 9.7	81.7 ± 10.7	0.28	82.4 ± 10.1	81.2 ± 11.0	0.08
Pulse pressure (mmHg)	54.3 ± 14.2	55.4 ± 14.4	0.34	55.0 ± 14.1	55.5 ± 14.9	0.61
HR (b.p.m.)	70.5 ± 10.8	72.0 ± 12.2	0.20	71.6 ± 11.3	71.7 ± 12.8	0.90
Smoking, n (%)	31 (15.1)	177 (23.1)	0.02	107 (18.0)	101 (26.7)	0.002
Physical inactivity, n (%)	90 (43.9)	318 (41.5)	0.59	257 (43.3)	151 (39.9)	0.33
BSA (m²)	1.75 ± 0.17	1.59 ± 0.16	<0.001	1.67 ± 0.17	1.55 ± 0.16	<0.001
BMI (kg/m²)	30.6 ± 2.7	23.9 ± 2.6	<0.001	27.0 ± 3.4	22.5 ± 2.6	<0.001
Waist circumference (cm)	99.9 ± 7.6	87.3 ± 7.8	<0.001	95.5 ± 6.8	81.3 ± 5.7	<0.001
Dyslipidaemia, n (%)	146 (83.4)	451 (73.3)	0.01	389 (78.4)	208 (70.7)	0.02
Diabetes mellitus, n (%)	65 (31.7)	151 (19.8)	<0.001	151 (25.5)	65 (17.2)	0.003
Hyperuricaemia, n (%)	151 (75.1)	463 (61.9)	<0.001	402 (69.1)	212 (57.8)	0.001
CKD, n (%)	24 (12.1)	100 (13.6)	0.65	76 (13.2)	48 (13.4)	1
FPG (mmol/L)	5.7 ± 1.4	5.3 ± 1.5	0.003	5.5 ± 1.5	5.2 ± 1.5	0.004
TC (mg/dL)	207.3 ± 57.8	212.1 ± 52.3	0.26	212.5 ± 54.0	208.9 ± 52.8	0.32
LDL-C (mg/dL)	124.9 ± 41.6	130.3 ± 37.4	0.19	130.4 ± 39.0	127.0 ± 37.3	0.34
HDL-C (mg/dL)	50.3 ± 19.4	54.4 ± 12.5	0.01	52.3 ± 14.9	55.5 ± 13.3	0.02
Triglyceride (mg/dL)[a]	160.8 [115.0, 237.8]	126.1 [91.5, 180.0]	<0.001	144.2 [105.2, 206.9]	115.0 [83.9, 166.8]	<0.001
Creatinine (μmol/L)	75.3 ± 27.6	80.4 ± 36.8	0.07	77.8 ± 30.0	81.6 ± 42.0	0.11
eGFR (mL/min/1.73 m²)	86.3 ± 24.7	82.8 ± 23.8	0.07	84.0 ± 25.2	83.0 ± 22.1	0.47
Uric acid (μmol/L)	460.5 ± 121.4	420.8 ± 123.6	<0.001	441.0 ± 124.1	410.6 ± 122.1	<0.001
Aspirin, n (%)	39 (19.0)	128 (16.7)	0.50	104 (17.5)	63 (16.7)	0.79
Statins, n (%)	76 (37.1)	196 (25.6)	0.002	176 (29.7)	96 (25.4)	0.17
Oral antidiabetics, n (%)	54 (26.3)	121 (15.8)	0.001	122 (20.6)	53 (14.0)	0.01
Insulin, n (%)	2 (1.0)	2 (0.3)	0.42	4 (0.7)	0 (0.0)	0.28
Allopurinol, n (%)	7 (3.4)	15 (2.0)	0.33	15 (2.5)	7 (1.9)	0.64
ACEI, n (%)	28 (13.7)	116 (15.1)	0.67	86 (14.5)	58 (15.3)	0.79
ARB, n (%)	115 (56.1)	374 (48.8)	0.08	323 (54.5)	166 (43.9)	0.002
CCB, n (%)	106 (51.7)	348 (45.4)	0.13	296 (49.9)	158 (41.8)	0.02
Diuretic, n (%)	35 (17.1)	102 (13.3)	0.21	90 (15.2)	47 (12.4)	0.27
Beta-blocker, n (%)	31 (15.1)	96 (12.5)	0.39	85 (14.3)	42 (11.1)	0.18

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; BSA, body surface area; CCB, calcium channel blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HR, heart rate; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol.

[a]Presented as median [Q1, Q3].

Table 2 Left ventricular structure and function comparisons according to general and abdominal obesity

Variables	General obesity (n = 205)	Non-general obesity (n = 766)	P-value	Abdominal obesity (n = 593)	Non-abdominal obesity (n = 378)	P-value
LV haemodynamics						
LVEDV (mL)	101.1 ± 25.8	90.1 ± 20.3	<0.001	95.3 ± 23.4	87.9 ± 18.7	<0.001
LVESV (mL)	32.7 ± 15.7	28.6 ± 11.2	<0.001	30.3 ± 13.5	28.1 ± 10.3	0.01
Stroke volume (mL)	68.4 ± 16.0	61.6 ± 13.7	<0.001	65.0 ± 15.3	59.8 ± 12.4	<0.001
LV structure						
IVS (mm)	10.1 ± 1.4	9.6 ± 1.3	<0.001	9.9 ± 1.3	9.4 ± 1.3	<0.001
PWT (mm)	9.9 ± 2.0	9.4 ± 1.8	<0.001	9.7 ± 1.8	9.3 ± 1.9	0.001
RWT	0.43 ± 0.09	0.43 ± 0.08	0.73	0.43 ± 0.08	0.43 ± 0.09	0.50
RWT > 0.42, n (%)	104 (50.7)	389 (50.8)	1	312 (52.6)	181 (47.9)	0.17
LVEDD (mm)	46.4 ± 4.9	44.3 ± 4.1	<0.001	45.3 ± 4.6	43.8 ± 3.9	<0.001
LVESD (mm)	28.7 ± 4.7	27.2 ± 3.9	<0.001	27.8 ± 4.4	27.1 ± 3.7	0.01
LVM (g)	164.3 ± 50.1	141.4 ± 38.3	<0.001	153.0 ± 44.8	135.5 ± 35.0	<0.001
LVM index (g/m^2)	94.2 ± 28.3	89.0 ± 22.4	0.01	91.6 ± 25.1	87.7 ± 21.6	0.01
LVH, n (%)	63 (30.7)	179 (23.4)	0.04	167 (28.2)	75 (19.8)	0.004
LVMV ratio (g/mL)	1.64 ± 0.33	1.58 ± 0.32	0.02	1.62 ± 0.31	1.56 ± 0.34	0.01
Left ventricular geometry						
Normal, n (%)	70 (34.1)	305 (39.8)	0.16	204 (34.4)	171 (45.2)	0.001
Concentric remodelling, n (%)	72 (35.1)	282 (36.8)	0.72	222 (37.4)	132 (34.9)	0.47
Concentric hypertrophy, n (%)	31 (15.1)	72 (9.4)	0.03	77 (13.0)	26 (6.9)	0.004
Eccentric hypertrophy, n (%)	32 (15.6)	107 (14.0)	0.63	90 (15.2)	49 (13.0)	0.39
LV systolic function						
LVEF (%)	67.4 ± 7.4	67.7 ± 7.0	0.56	67.6 ± 7.6	67.7 ± 6.2	0.81
Septal S' velocity (cm/s)	6.35 ± 1.48	6.40 ± 1.56	0.66	6.40 ± 1.57	6.38 ± 1.49	0.78
LV diastolic function						
Peak E-wave velocity (m/s)	0.73 ± 0.26	0.67 ± 0.19	<0.001	0.69 ± 0.23	0.68 ± 0.17	0.49
Peak A-wave velocity (m/s)	0.90 ± 0.25	0.86 ± 0.17	0.04	0.89 ± 0.20	0.85 ± 0.18	0.002
E/A ratio	0.83 ± 0.27	0.80 ± 0.25	0.12	0.79 ± 0.24	0.83 ± 0.27	0.01
LA volume (mL)	50.8 ± 20.5	40.7 ± 20.6	<0.001	45.5 ± 21.6	38.7 ± 19.4	<0.001
LA volume index (mL/m^2)	29.3 ± 11.9	25.8 ± 13.5	0.001	27.4 ± 13.3	25.2 ± 13.0	0.01
LA volume index > 34 mL/m^2, n (%)	53 (26.2)	127 (16.8)	0.003	122 (20.9)	58 (15.4)	0.04
Septal E/e' ratio	14.8 ± 7.8	13.1 ± 4.4	<0.001	14.0 ± 5.9	12.6 ± 4.3	<0.001
Septal E/e' ratio > 15, n (%)	79 (38.5)	194 (25.4)	<0.001	188 (31.8)	85 (22.5)	0.002
Septal e' velocity (cm/s)	5.39 ± 1.79	5.49 ± 1.74	0.48	5.25 ± 1.60	5.80 ± 1.91	<0.001
Septal e' velocity < 7 cm/s, n (%)	155 (75.6)	573 (74.8)	0.88	470 (79.3)	258 (68.3)	<0.001

IVS, interventricular septum thickness; LA, left atrial; LV, left ventricular; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; LVH, left ventricular hypertrophy; LVM, left ventricular mass; LVMV, left ventricular mass-to-volume; PWT, posterior wall thickness; RWT, relative wall thickness.

Figure 2 Trends in left ventricular structure and function according to the quartiles of BMI and WC. There was a trend in increasing LVEDV, SV, LVM, LVMV ratio, left atrial volume, and septal E/e' ratio with increasing BMI and WC; and there was a trend in decreasing septal e' velocity with increasing WC. No significant trend in LVEF and septal S' velocity with increasing BMI and WC. BMI: the first quartile (20.8 ± 1.6 kg/m^2, *n* = 243), the second quartile (23.9 ± 0.6 kg/m^2, *n* = 242), the third quartile (26.2 ± 0.80 kg/m^2, *n* = 242), and the fourth quartile (30.1 ± 2.7 kg/m^2, *n* = 244). WC: the first quartile (78.1 ± 4.7 cm, *n* = 237), the second quartile (86.8 ± 1.7 cm, *n* = 238), the third quartile (92.3 ± 1.9 cm, *n* = 244), and the fourth quartile (102 ± 5.4 cm, *n* = 252). BMI, body mass index; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; LVMV, left ventricular mass-to-volume; SV, stroke volume; WC, waist circumference.
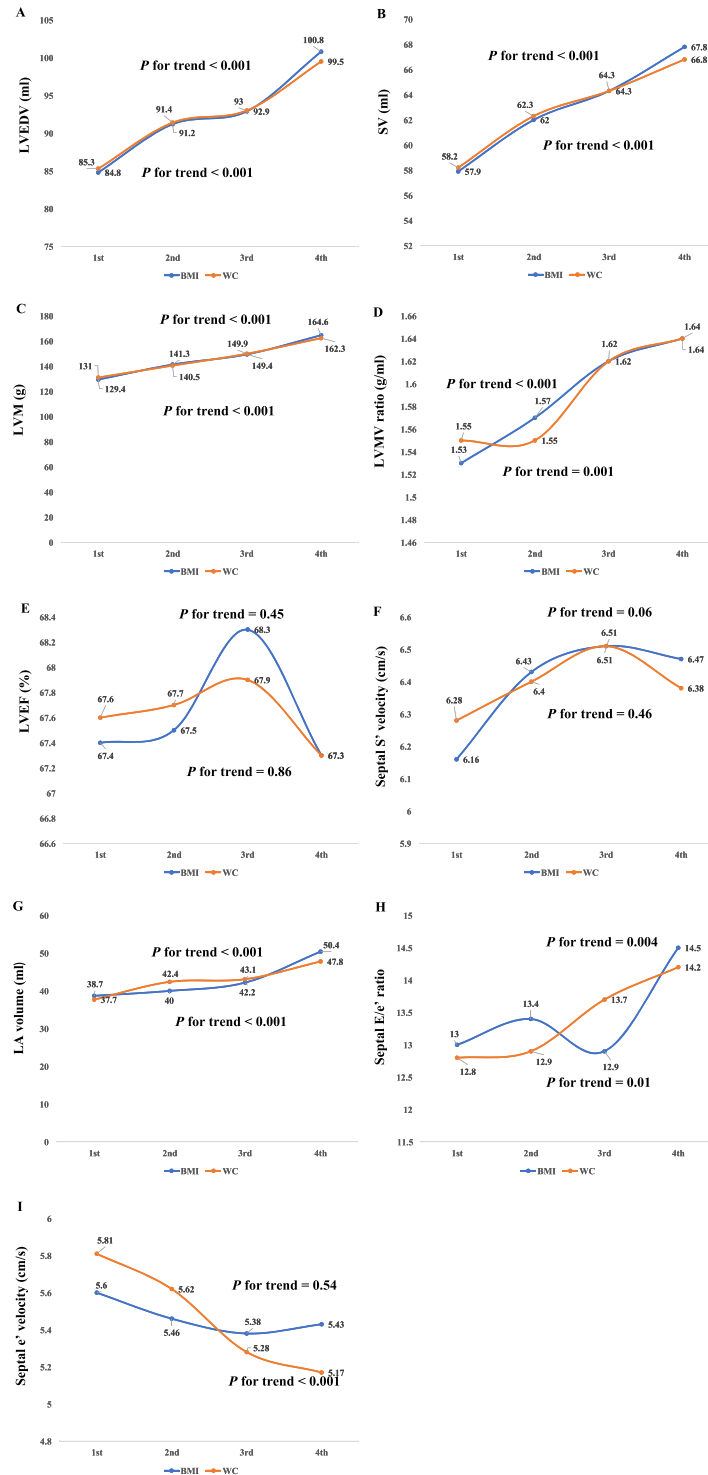
Figure 3 Correlation between body mass index and waist circumference with metabolic factors and blood pressure. (A) Body mass index was positively correlated with fasting plasma glucose, triglyceride, and diastolic blood pressure, while negatively correlat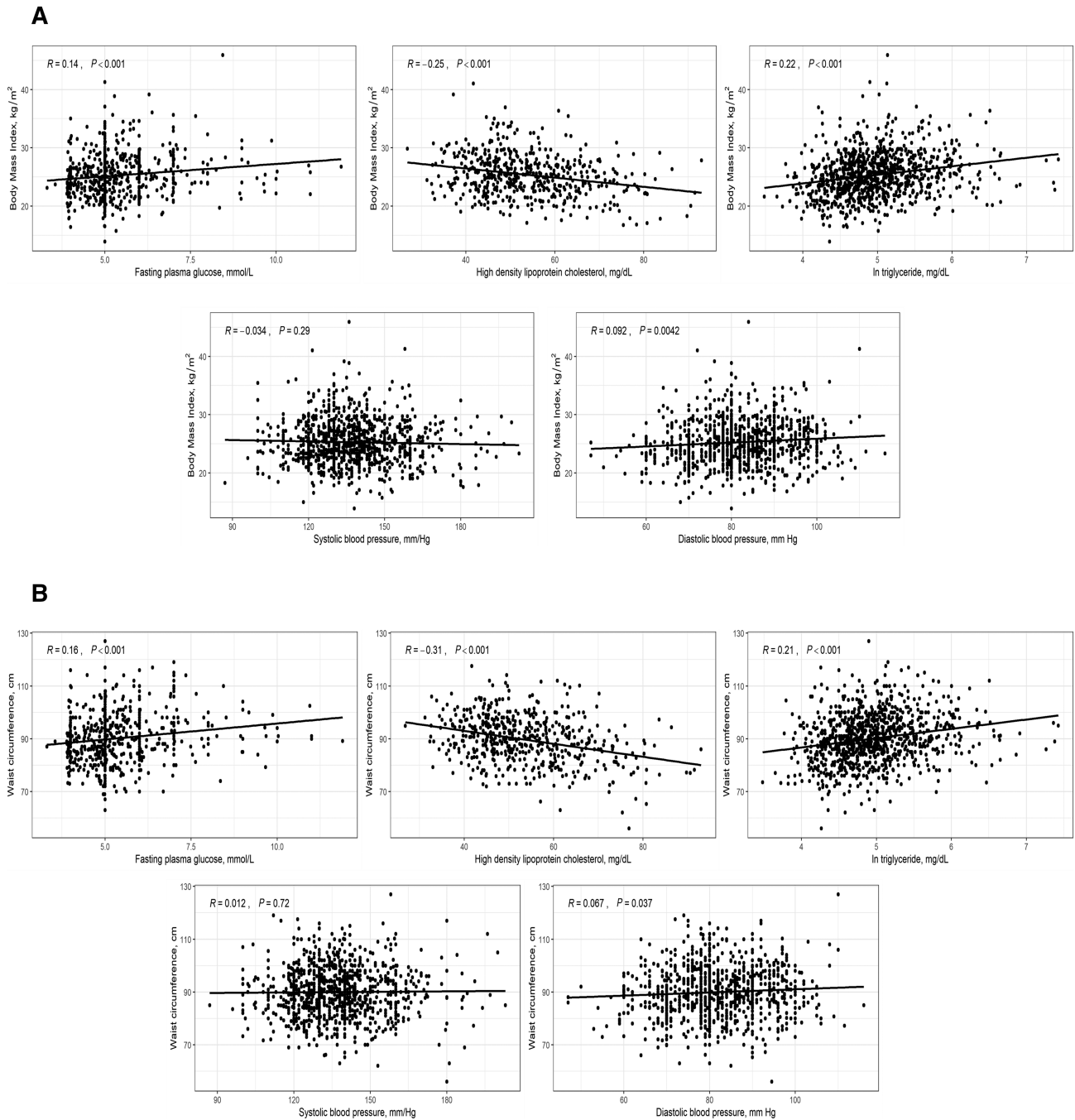ed with high-density lipoprotein cholesterol. (B) Waist circumference was positively correlated with fasting plasma glucose, triglyceride, and diastolic blood pressure, while negatively correlated with high-density lipoprotein cholesterol.

Table 3 Association between general and abdominal obesity with selected indices of left ventricular structure and function

General obesity (yes vs. no)	Unadjusted β (95% CI)	P-value	Model 1 β (95% CI)	P-value	Model 2 β (95% CI)	P-value
LVEDV (mL)	10.96 (7.63, 14.28)	<0.001	10.85 (7.16, 14.54)	<0.001	4.65 (0.37, 8.93)	0.03
SV (mL)	8.21 (5.03, 11.40)	<0.001	7.44 (3.70, 11.18)	<0.001	3.61 (−0.80, 8.02)	0.11
LVM (g)	22.93 (16.59, 29.27)	<0.001	23.71 (16.64, 30.78)	<0.001	10.04 (1.89, 18.18)	0.02
LVMV ratio (g/mL)	0.06 (0.01, 0.11)	0.02	0.07 (0.01, 0.12)	0.03	0.02 (−0.05, 0.09)	0.52
LVEF (%)	−0.32 (−1.41, 0.77)	0.56	−0.51 (−1.79, 0.77)	0.43	−0.35 (−1.86, 1.17)	0.65
Septal S' (m/s)	−0.05 (−0.29, 0.19)	0.66	−0.19 (−0.45, 0.06)	0.14	−0.25 (−0.55, 0.06)	0.11
LA volume (mL)	10.07 (6.87, 13.27)	<0.001	9.75 (6.45, 13.04)	<0.001	5.90 (2.01, 9.79)	<0.001
Septal E/e' ratio	1.77 (0.95, 2.60)	<0.001	2.02 (1.10, 2.94)	<0.001	1.49 (0.40, 2.57)	0.007
Septal e' velocity (cm/s)	−0.10 (−0.37, 0.17)	0.48	−0.29 (−0.55, −0.02)	0.04	0.10 (−0.21, 0.41)	0.53

Abdominal obesity (yes vs. no)	Unadjusted β (95% CI)	P-value	Model 1 β (95% CI)	P-value	Model 2 β (95% CI)	P-value
LVEDV (mL)	7.42 (4.62, 10.22)	<0.001	9.63 (6.46, 12.80)	<0.001	3.39 (−0.33, 7.11)	0.07
SV (mL)	4.88 (2.27, 7.49)	<0.001	4.97 (1.84, 8.10)	0.002	0.65 (−2.90, 4.20)	0.72
LVM (g)	17.49 (12.16, 22.82)	<0.001	21.18 (15.11, 27.25)	<0.001	6.41 (−0.63, 13.44)	0.07
LVMV ratio (g/mL)	0.06 (0.02, 0.10)	0.005	0.06 (0.01, 0.11)	0.02	0.01 (−0.05, 0.07)	0.71
LVEF (%)	−0.12 (−1.03, 0.80)	0.81	−0.69 (−1.79, 0.41)	0.22	−0.76 (−2.08, 0.57)	0.26
Septal S' (m/s)	0.03 (−0.17, 0.23)	0.78	0.06 (−0.16, 0.28)	0.59	0.12 (−0.14, 0.39)	0.36
LA volume (mL)	6.77 (4.08, 9.46)	<0.001	6.86 (4.01, 9.71)	<0.001	1.00 (−2.37, 4.36)	0.56
Septal E/e' ratio	1.34 (0.65, 2.03)	<0.001	1.31 (0.51, 2.11)	0.001	0.53 (−0.42, 1.48)	0.28
Septal e' velocity (cm/s)	−0.55 (−0.77, −0.33)	<0.001	−0.52 (−0.75, −0.29)	<0.001	−0.34 (−0.61, −0.07)	0.01

CI, confidence interval; LA, left atrial; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; LVMV, left ventricular mass-to-volume; SV, stroke volume.
Model 1: adjusting for age, sex, smoking, physical inactivity, systolic blood pressure, dyslipidaemia, diabetes mellitus, estimated glomerular filtration rate, uric acid, and antihypertensive drugs. Model 2 in general obesity: Model 1 plus waist circumference. Model 2 in abdominal obesity: Model 1 plus body mass index.

Table 4 Association between general and abdominal obesity with selected indices of left ventricular structure and function by sex

	General obesity β (95% CI)	P-interaction	Abdominal obesity β (95% CI)	P-interaction
LEVDV				
Men	6.22 (−1.81, 14.26)	0.18	6.99 (−0.01, 13.98)	0.19
Women	3.94 (−1.03, 8.91)		1.25 (−3.11, 5.61)	
SV				
Men	4.68 (−3.15, 12.52)	0.57	1.41 (−5.13, 7.94)	0.59
Women	2.60 (−2.82, 8.03)		−0.08 (−4.37, 4.21)	
LVM				
Men	5.57 (−9.72, 20.86)	0.92	21.20 (8.03, 34.36)	0.04
Women	12.65 (3.18, 22.13)		−1.56 (−9.78, 6.66)	
LVMV ratio				
Men	−0.05 (−0.17, 0.07)	0.18	0.11 (0, 0.21)	0.20
Women	0.06 (−0.02, 0.15)		−0.04 (−0.11, 0.04)	
LA volume				
Men	0.61 (−5.96, 7.17)	0.26	0.93 (−4.71, 6.57)	0.88
Women	9.05 (4.23, 13.88)		0.89 (−3.38, 5.15)	
Septal E/e' ratio				
Men	1.26 (−0.68, 3.20)	0.45	0.75 (−0.92, 2.42)	0.22
Women	1.58 (0.28, 2.89)		0.24 (−0.92, 1.41)	
Septal e' velocity				
Men	0.16 (−0.38, 0.70)	0.18	−0.58 (−1.04, −0.12)	<0.001
Women	0.02 (−0.35, 0.40)		−0.11 (−0.45, 0.22)	

CI, confidence interval; LA, left atrial; LVEDV, left ventricular end-diastolic volume; LVM, left ventricular mass; LVMV, left ventricular mass-to-volume; SV, stroke volume.
Adjusting for age, smoking, physical inactivity, systolic blood pressure, dyslipidaemia, diabetes mellitus, estimated glomerular filtration rate, uric acid, and antihypertensive drugs; waist circumference in general obesity; or body mass index in abdominal obesity.

stressing the importance of incorporating BMI and WC measurements into assessing obesity-related LV alteration by sex.

Differences in body composition according to ethnicity

Body composition is varied significantly according to different ethnic groups. For example, Wang *et al.* compared body composition between Chinese and White men who live in China.[17] After adjusting for age and BMI, Chinese men had significantly higher percentage of body fat including whole body and the trunk area compared with their white counterparts, suggesting that Chinese men had more body fat and a greater degree of central fat deposition pattern.[17] Lear *et al.* evaluated the relationship between BMI and total body fat and subcutaneous and visceral adipose tissue across different ethnic groups. The findings suggest that BMI significantly underestimated visceral adipose tissue in Chinese and other groups, and when a total body fat > 9.1 kg, the Chinese group had a higher amount of visceral adipose tissue than the other groups.[32] Results from Deurenberg-Yap *et al.* suggested that Singaporeans have a higher body fat percentage at a lower BMI compared with Caucasians, and if obesity is defined as excess body fat rather than excess weight, a lower BMI cut-off point should be used for Singaporeans.[33] Compared with Caucasians and other ethnic groups, Asian Indians had more fat, both total and in the abdominal region, with less lean mass and skeletal muscle.[34] Collectively, the evidence demonstrates that given a certain BMI, the Asians have a higher total body fat and subcutaneous adipose tissue compared with their Caucasian counterparts.[35,36]

Left ventricular haemodynamics and structure among individuals with general and abdominal obesity

Consistent to prior studies,[6–11] results of the current study showed that individuals with general and abdominal obesity had a higher central blood volume and cardiac output, which predisposed to increasing LV wall stress and LVM. Although initial studies have suggested that obesity was associated with eccentric remodelling due to chronic volume overload,[37,38] results of recent and the current studies showed that obese individuals were more likely to develop concentric remodelling. Several mechanisms,[39–42] including activations of sympathetic nervous system and renin–angiotensin–aldosterone system, increased pressure overload (e.g. BP elevation), insulin-resistant, hyperleptinaemia, and increased release of insulin-related growth factors, have been proposed to explain the obesity-related LV concentric remodelling and hypertrophy.

Studies have evaluated the relationship between measures of obesity and LV geometry. Lee *et al.* reported that when BMI, WC, and clinical factors were included in the multivariable model, both BMI and WC were associated with LVM.[10] Turkbey *et al.* reported that both increased BMI and WC were positively associated with LVMV ratio, an index of concentric remodelling.[7] In the current study, general obesity was only associated with LVM after adjusting for WC, while there was no relationship between abdominal obesity and LVM or LVMV ratio after adjusting for BMI. Importantly, when we evaluated the relationship between BMI and LV geometry, the results suggested that BMI was still associated with LVM and LVMV ratio after adjusting for WC. Nonetheless, there remained no association between WC with LVM and LVMV ratio after adjusting for BMI. One of the possible explanations was that compared with per 1 cm increase in WC, per 1 kg/m^2 increase in BMI was associated with a larger increase in LVEDV and SV (Supporting Information, *Table S1*), which in turn resulted in a greater increase in LV wall stress and LVM, and concentric remodelling.[42] From this perspective, compared with WC (an index of regional fat mass), BMI (an index of general body mass) might be more closely related to LV haemodynamics and structural alterations.

Left ventricular systolic function among individuals with general and abdominal obesity

The reports on the relationship between obesity and LV systolic dysfunction were conflicting.[7,8,12,43–49] Differences in the diagnostic techniques in assessing LV systolic function, obese duration and severity, and clinical characteristics of participants might explain these discrepancies. In the current study, the LVEF was within normal range among all participants, and the mean LVEF did not differ by general and abdominal obese status. In addition, there was no significant trend in LVEF alteration with increasing BMI and WC. There was also no relationship between general and abdominal obesity with LVEF, neither BMI nor WC with LVEF. Similar findings were observed when less load-dependent index of LV systolic function (septal S' velocity) was analysed. Nonetheless, when individuals already have LV systolic dysfunction, coexistent obesity might result in further deterioration of LV systolic performance due to obesity-related blood volume augmentation, chronic inflammation, neurohormonal activation, and among others. Taken together, findings of the current study suggested that obesity was not associated with LV systolic dysfunction as assessed by LVEF and septal S' velocity among hypertensive individuals without overt cardiovascular disease.

Left ventricular diastolic function among individuals with general and abdominal obesity

Concentric remodelling, LVH, and impaired LV relaxation predispose obese individuals, to developing LV diastolic dysfunction.[42,50,51] Indeed, the current study showed that obese individuals, regardless of general or abdominal, had a higher LA volume and septal E/e' ratio and a lower septal e' velocity than their non-obese counterparts. In addition, obesity was significantly associated with these alterations even after adjusting for relevant clinical covariates. Findings from prior studies also support the relationship between obesity and LV diastolic dysfunction.[8,9,12,13,52] The novelty of the current study was that we assessed and compared the alterations of LV diastolic function in association with different forms of adipose tissue distribution (general vs. abdominal). Interestingly and importantly, after accounting for WC, general obesity was associated with increased LA volume and septal E/e' ratio, while abdominal obesity was associated with reduced septal e' velocity after accounting for BMI. Notably, LA volume and septal E/e' ratio are sensitive markers of LV filling status, and septal e' velocity is a marker of LV relaxation.[31] These results might reflect the differential mechanisms by which general and abdominal obesity contribute to LV diastolic dysfunction. For example, increased abdominal fat mass is associated with dysglycaemia, dyslipidaemia, chronic inflammation, and endothelial dysfunction, which in turn might impair LV relaxation. In contrast, increased general body mass was more relevant to blood volume augmentation and concentric remodelling, which in turn might increase LV filling pressure. Taken together, these results suggest that general and abdominal obesity play complement roles in LV diastolic dysfunction.

Relationship between left ventricular structure and function with general and abdominal obesity by sex

Compared with men, women were more likely to develop HFpEF.[23–25] Sex differences in both the risk factors and their associated influences on cardiovascular systems have been proposed to explain these observations.[23–25] Nonetheless, whether general and abdominal obesity had differential influences on LV structure and function among hypertensive individuals without overt cardiovascular diseases is unknown. With ageing, women are more likely than their male counterparts to gain fat mass and develop abdominal obesity.[53,54] Therefore, one might speculate that obesity might have worse impacts on LV structure and function in women. Importantly, findings of the current study showed that general obesity was significantly associated with LVM, LA volume, and septal E/e' ratio only in women; however, the interaction analysis did not achieve statistical significance. In contrast, abdominal obesity had worse impacts on LVM and septal e' velocity in men. We were unsure the mechanisms and further studies are needed to corroborate our findings.

Clinical implication

There are three important clinical implications. First, findings of the current study reinforce the need and importance of incorporating BMI and WC measurements in routine clinical practice. Second, recognizing the different patterns of LV alterations in association with different forms of adipose tissue distribution, measuring BMI and WC may help physicians to predict LV alterations in a convenient way. Third, sex should be taken into consideration when evaluating the obesity-related LV structural and functional alterations.

Limitations

There are several limitations of the current study. First, this is an observational study, and no causal relationship between obesity and LV alterations should be drawn. Second, this is a study of Chinese community populations, and findings of the current study should not be extrapolated to other ethnic groups. Third, the relatively small sample size of the current study might compromise the statistical power to detect some significant differences in the interaction analysis. Fourth, although we have adjusted for multiple covariates, unknown and unmeasured covariates might still exist and influence the relationship between obesity and LV structure and function.

Conclusions

In conclusion, findings of the current study suggest that among Chinese hypertensive individuals without overt cardiovascular disease, general and abdominal obesity were associated with different patterns of LV structural and functional alterations, which were modified by sex.

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Conflict of interest

None declared.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Association between BMI and WC with indices of LV structure and function.

References

1. Zhang X, Zhang M, Zhao Z, Huang Z, Deng Q, Li Y, Pan A, Li C, Chen Z, Zhou M, Yu C, Stein A, Jia P, Wang L. Geographic variation in prevalence of adult obesity in China: results from the 2013–2014 National Chronic Disease and Risk Factor Surveillance. *Ann Intern Med* 2020; **172**: 291–293.

2. Zhang L, Wang Z, Wang X, Chen Z, Shao L, Tian Y, Zheng C, Li S, Zhu M, Gao R, China Hypertension Survey Investigators. Prevalence of overweight and obesity in China: results from a cross-sectional study of 441 thousand adults, 2012–2015. *Obes Res Clin Pract* 2020; **14**: 119–126.

3. Zhang L, Wang Z, Wang X, Chen Z, Shao L, Tian Y, Dong Y, Zheng C, Li S, Zhu M, Gao R. Prevalence of abdominal obesity in China: results from a cross-sectional study of nearly half a million participants. *Obesity (Silver Spring, Md.)* 2019; **27**: 1898–1905.

4. Ma S, Xi B, Yang L, Sun J, Zhao M, Bovet P. Trends in the prevalence of overweight, obesity, and abdominal obesity among Chinese adults between 1993 and 2015. *Int J Obes (Lond)* 2021; **45**: 427–437.

5. Chen Y, Peng Q, Yang Y, Zheng S, Wang Y, Lu W. The prevalence and increasing trends of overweight, general obesity, and abdominal obesity among Chinese adults: a repeated cross-sectional study. *BMC Public Health* 2019; **19**: 1293.

6. Wohlfahrt P, Redfield MM, Lopez-Jimenez F, Melenovsky V, Kane GC, Rodeheffer RJ, Borlaug BA. Impact of general and central adiposity on ventricular-arterial aging in women and men. *JACC He fai* 2014; **2**: 489–499.

7. Turkbey EB, McClelland RL, Kronmal RA, Burke GL, Bild DE, Tracy RP, Arai AE, Lima JA, Bluemke DA. The impact of obesity on the left ventricle: the Multi-Ethnic Study of Atherosclerosis (MESA). *J Am Coll Cardiol Img* 2010; **3**: 266–274.

8. Selvaraj S, Martinez EE, Aguilar FG, Kim KYA, Peng J, Sha J, Irvin MR, Lewis CE, Hunt SC, Arnett DK, Shah SJ. Association of central adiposity with adverse cardiac mechanics: findings from the Hypertension Genetic Epidemiology Network study. *Circ Cardiovasc Imaging* 2016; **9**: e004396.

9. Russo C, Jin Z, Homma S, Rundek T, Elkind MSV, Sacco RL, di Tullio MR. Effect of obesity and overweight on left ventricular diastolic function: a community-based study in an elderly cohort. *J Am Coll Cardiol* 2011; **57**: 1368–1374.

10. Lee TC, Jin Z, Homma S, Nakanishi K, Elkind MSV, Rundek T, Tugcu A, Matsumoto K, Sacco RL, di Tullio MR. Changes in left ventricular mass and geometry in the older adults: role of body mass and central obesity. *J Ame Soc Echocardio: official pub Ame Soc Echocardi* 2019; **32**: 1318–1325.

11. van Hout MJP, Dekkers IA, Westenberg JJM, Schalij MJ, Scholte A, Lamb HJ. The impact of visceral and general obesity on vascular and left ventricular function and geometry: a cross-sectional magnetic resonance imaging study of the UK Biobank. *Eur Heart J Cardiovasc Imaging* 2020; **21**: 273–281.

12. Ammar KA, Redfield MM, Mahoney DW, Johnson M, Jacobsen SJ, Rodeheffer RJ. Central obesity: association with left ventricular dysfunction and mortality in the community. *Am Heart J* 2008; **156**: 975–981.

13. Canepa M, Strait JB, Abramov D, Milaneschi Y, AlGhatrif M, Moni M, Ramachandran R, Najjar SS, Brunelli C, Abraham TP, Lakatta EG, Ferrucci L. Contribution of central adiposity to left ventricular diastolic function (from the Baltimore Longitudinal Study of Aging). *Am J Cardiol* 2012; **109**: 1171–1178.

14. Elagizi A, Carbone S, Lavie CJ, Mehra MR, Ventura HO. Implications of obesity across the heart failure continuum. *Prog Cardiovasc Dis* 2020; **63**: 561–569.

15. Yildiz M, Oktay AA, Stewart MH, Milani RV, Ventura HO, Lavie CJ. Left ventricular hypertrophy and hypertension. *Prog Cardiovasc Dis* 2020; **63**: 10–21.

16. Heymsfield SB, Peterson CM, Thomas DM, Heo M, Schuna JM Jr. Why are there race/ethnic differences in adult body mass index-adiposity relationships? A quantitative critical review. *Obe rev: an offi j Intern Asso Stu Obe* 2016; **17**: 262–275.

17. Wang D, Li Y, Lee SG, Wang L, Fan J, Zhang G, Wu J, Ji Y, Li S. Ethnic differences in body composition and obesity related risk factors: study in Chinese and white males living in China. *PLoS ONE* 2011; **6**: e19835.

18. Rush EC, Goedecke JH, Jennings C, Micklesfield L, Dugas L, Lambert EV, Plank LD. BMI, fat and muscle differences in urban women of five ethnicities from two countries. *Intern j obe (2005)* 2007; **31**: 1232–1239.

19. Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. *Obe rev: an official j Intern Assoc Stu Obe* 2002; **3**: 141–146.

20. Pan WH, Flegal KM, Chang HY, Yeh WT, Yeh CJ, Lee WC. Body mass index and obesity-related metabolic disorders in Taiwanese and US whites and blacks: implications for definitions of overweight and obesity for Asians. *Am J Clin Nutr* 2004; **79**: 31–39.

21. Lai CL, Chien KL, Hsu HC, Su TC, Chen MF, Lee YT. Left ventricular mass and risk of cardiovascular events and all-cause death among ethnic Chinese—the Chin-Shan Community Cardiovascular Cohort study. *Int J Cardiol* 2011; **149**: 347–352.

22. Echocardiographic Normal Ranges Meta-Analysis of the Left Heart Collaboration. Ethnic-specific normative

reference values for echocardiographic LA and LV size, LV mass, and systolic function: the EchoNoRMAL study. *J Am Coll Cardiol Img* 2015; **8**: 656–665.

23. Beale AL, Meyer P, Marwick TH, Lam CSP, Kaye DM. Sex differences in cardiovascular pathophysiology: why women are overrepresented in heart failure with preserved ejection fraction. *Circulation* 2018; **138**: 198–205.

24. Stolfo D, Uijl A, Vedin O, Strömberg A, Faxén J, Rosano GMC, Sinagra G, Dahlström U, Savarese G. Sex-based differences in heart failure across the ejection fraction spectrum: phenotyping, and prognostic and therapeutic implications. *JACC Heart fail* 2019; **7**: 505–515.

25. Lam CS, Arnott C, Beale AL, Chandramouli C, Hilfiker-Kleiner D, Kaye DM, Ky B. Sex differences in heart failure. *Eur Heart J* 2019; **40**: 3859–3868c.

26. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, Kusek JW, van Lente F, Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med* 2006; **145**: 247–254.

27. Cai A, Liu L, Siddiqui M, Zhou D, Chen J, Calhoun DA, Tang S, Zhou Y, Feng Y. Uric acid is not associated with blood pressure phenotypes and target organ damage according to blood pressure phenotypes. *Am J Hypertens* 2020.

28. Joint Committee for Guideline Revision. 2018 Chinese Guidelines for Prevention and Treatment of Hypertension—a report of the Revision Committee of Chinese Guidelines for Prevention and Treatment of Hypertension. *J Geriatr Cardiol: JGC* 2019; **16**: 182–241.

29. Consultation WHOE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet (London, England)* 2004; **363**: 157–163.

30. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Ame Soc Echocardio: official pub Ame Soc Echocardi* 2015; **28**: 1–39.e14.

31. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF III, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, Marino P, Oh JK, Popescu BA, Waggoner AD. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Ame Soc Echocardiog: official publ Ame Soc Echocardio* 2016; **29**: 277–314.

32. Lear SA, Humphries KH, Kohli S, Chockalingam A, Frohlich JJ, Birmingham CL. Visceral adipose tissue accumulation differs according to ethnic background: results of the Multicultural Community Health Assessment Trial (M-CHAT). *Am J Clin Nutr* 2007; **86**: 353–359.

33. Deurenberg-Yap M, Schmidt G, van Staveren WA, Deurenberg P. The paradox of low body mass index and high body fat percentage among Chinese, Malays and Indians in Singapore. *Intern j obes related metab disord: j Intern Assoc Stu Obe* 2000; **24**: 1011–1017.

34. Rush EC, Freitas I, Plank LD. Body size, body composition and fat distribution: comparative analysis of European, Maori, Pacific Island and Asian Indian adults. *Br J Nutr* 2009; **102**: 632–641.

35. Wulan SN, Westerterp KR, Plasqui G. Ethnic differences in body composition and the associated metabolic profile: a comparative study between Asians and Caucasians. *Maturitas* 2010; **65**: 315–319.

36. Haldar S, Chia SC, Henry CJ. Body composition in Asians and Caucasians: comparative analyses and influences on cardiometabolic outcomes. *Adv Food Nutr Res* 2015; **75**: 97–154.

37. Messerli FH, Sundgaard-Riise K, Reisin ED, Dreslinski GR, Ventura HO, Oigman W, Frohlich ED, Dunn FG. Dimorphic cardiac adaptation to obesity and arterial hypertension. *Ann Intern Med* 1983; **99**: 757–761.

38. Alpert MA, Karthikeyan K, Abdullah O, Ghadban R. Obesity and cardiac remodeling in adults: mechanisms and clinical implications. *Prog Cardiovasc Dis* 2018; **61**: 114–123.

39. Harmancey R, Wilson CR, Taegtmeyer H. Adaptation and maladaptation of the heart in obesity. *Hypertension (Dallas, Tex: 1979)* 2008; **52**: 181–187.

40. Wong C, Marwick TH. Obesity cardiomyopathy: pathogenesis and pathophysiology. *Nat Clin Pract Cardiovasc Med* 2007; **4**: 436–443.

41. Mouton AJ, Li X, Hall ME, Hall JE. Obesity, hypertension, and cardiac dysfunction: novel roles of immunometabolism in macrophage activation and inflammation. *Circ Res* 2020; **126**: 789–806.

42. Aurigemma GP, de Simone G, Fitzgibbons TP. Cardiac remodeling in obesity. *Circ Cardiovasc Imaging* 2013; **6**: 142–152.

43. Pascual M, Pascual DA, Soria F, Vicente T, Hernández AM, Tébar FJ, Valdés M. Effects of isolated obesity on systolic and diastolic left ventricular function. *Heart (British Cardiac Society)* 2003; **89**: 1152–1156.

44. Tumuklu MM, Etikan I, Kisacik B, Kayikcioglu M. Effect of obesity on left ventricular structure and myocardial systolic function: assessment by tissue Doppler imaging and strain/strain rate imaging. *Echocardiography (Mount Kisco, NY)* 2007; **24**: 802–809.

45. Peterson LR, Waggoner AD, Schechtman KB, Meyer T, Gropler RJ, Barzilai B, Dávila-Román VG. Alterations in left ventricular structure and function in young healthy obese women: assessment by echocardiography and tissue Doppler imaging. *J Am Coll Cardiol* 2004; **43**: 1399–1404.

46. Scaglione R, Dichiara MA, Indovina A, Lipari R, Ganguzza A, Parrinello G, Capuana G, Merlino G, Licata G. Left ventricular diastolic and systolic function in normotensive obese subjects: influence of degree and duration of obesity. *Eur Heart J* 1992; **13**: 738–742.

47. Snelder SM, de Groot-de Laat LE, Biter LU, Castro Cabezas M, Pouw N, Birnie E, Boxma-de Klerk BM, Klaassen RA, Zijlstra F, van Dalen BM. Subclinical cardiac dysfunction in obesity patients is linked to autonomic dysfunction: findings from the CARDIOBESE study. *ESC heart failure* 2020; **7**: 3726–3737.

48. Buddeberg BS, Fernandes NL, Vorster A, Cupido BJ, Lombard CJ, Swanevelder JL, Girard T, Dyer RA. Cardiac structure and function in morbidly obese parturients: an echocardiographic study. *Anesth Analg* 2019; **129**: 444–449.

49. Bello NA, Cheng S, Claggett B, Shah AM, Ndumele CE, Roca GQ, Santos AB, Gupta D, Vardeny O, Aguilar D, Folsom AR. Association of weight and body composition on cardiac structure and function in the ARIC study (Atherosclerosis Risk in Communities). *Circ Heart Fail* 2016; **9**.

50. Neeland IJ, Gupta S, Ayers CR, Turer AT, Rame JE, Das SR, Berry JD, Khera A, McGuire DK, Vega GL, Grundy SM, de Lemos JA, Drazner MH. Relation of regional fat distribution to left ventricular structure and function. *Circ Cardiovasc Imaging* 2013; **6**: 800–807.

51. Alpert MA, Lavie CJ, Agrawal H, Kumar A, Kumar SA. Cardiac effects of obesity: pathophysiologic, clinical, and prognostic consequences—a review. *J Cardiopulm Rehabil Prev* 2016; **36**: 1–11.

52. Libhaber CD, Norton GR, Majane OH, Libhaber E, Essop MR, Brooksbank R, Maseko M, Woodiwiss AJ. Contribution of central and general adiposity to abnormal left ventricular diastolic function in a community sample with a high prevalence of obesity. *Am J Cardiol* 2009; **104**: 1527–1533.

53. Wells JC. Sexual dimorphism of body composition. *Best Pract Res Clin Endocrinol Metab* 2007; **21**: 415–430.

54. Bredella MA. Sex differences in body composition. *Adv Exp Med Biol* 2017; **1043**: 9–27.