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RESEARCH ARTICLE

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Prevalence of and risk factors for abnormal left ventricular geometrical patterns in hypertensive subjects administered irbesartan

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Abstract

Background: Distinct populations differ in LVH prevalence and impaired LV geometry. Currently, the prevalence of and risk factors for LV geometric patterns in Chinese hypertensives administered irbesartan have not been specifically addressed in large studies.

Methods: Totally 10,883 patients (6623 men and 4260 women) completed the survey, including 1181 hypertensives administered irbesartan (488 males and 693 females) that were finally enrolled. Based on LVMI and RWT derived from comprehensive echocardiography, the LV geometric patterns of irbesartan-treated hypertensive individuals were classified into four types, including the normal, concentric remodeling, and concentric and eccentric hypertrophy groups. Logistic regression analysis was applied in males and females, respectively, for determining odds ratios (ORs) and 95% confidence intervals (CIs) for various potential risk factors for abnormal LV geometrical patterns in irbesartan-treated hypertensives.

Results: The clinical and echocardiographic data differed significantly between males and females. The prevalence rates of concentric remodeling, concentric hypertrophy, and eccentric hypertrophy were 36.3%, 15.4%, and 6.1% in males, respectively, and 23.5%, 20.3%, and 23.8% in females, accordingly. Gender, daily dose of irbesartan, BMI, SBP, WtHR, and neck-circumference were significantly associated with LV geometric patterns. After adjustment for confounding factors, risk factors for LVH and impaired LV geometry included SBP, WtHR in males, and MAU-Cr and WtHR in females.

Conclusions: LVH and impaired LV geometric patterns are more prevalent in females (67.7%) compared with that in males (57.8%) among hypertensives upon irbesartan administration. For such population, risk factors beyond elevated blood pressure may be involved in the progression of LVH and impaired LV geometric patterns in both genders.

KEYWORDS
irbesartan-treated hypertension, left ventricular geometry, left ventricular hypertrophy LVH, LVMI, risk factors, RWT

1 | INTRODUCTION

Cardiovascular disease constitutes a major cause of death across the world, representing an enormous public health threat in both developed and developing countries. Of note, left ventricular hypertrophy and geometrical abnormalities are significantly associated with cardiovascular risk factors, and independently predict myocardial ischemia,[1] coronary disease,[2] congestive heart failure,[3] ventricular arrhythmias,[4] cardiac mortality,[5] ischemic stroke,[6] and sudden cardiac death.[7] Therefore, the left ventricular (LV) geometric pattern represents a critical prognostic factor in cardiovascular disease.

Based on LV mass index (LVMI) and relative wall thickness (RWT), according to echocardiography data, the left ventricular geometrical patterns were classified into four types, including the normal, concentric remodeling, and eccentric and concentric hypertrophies,[8] with progressive geometry impairment. Interestingly, it is known that echocardiography-derived LV geometry independently predicts cardiovascular disease.[9] Besides, LV geometric pattern shows a close association with stroke risk.[10]

Cardiac hypertrophy and geometrical abnormalities are considered an adaptive response to enhanced workload. Nevertheless, both clinical and animal studies revealed that the extents of cardiac hypertrophy and remodeling are not proportionally associated with workload.[11] Overactivation of the renin-angiotensin system has been found to be involved in hypertrophic remodeling modulation, which is consistent with increasing evidence that plasma aldosterone levels are elevated in cardiovascular disease.[12,13] Importantly, angiotensin receptor blockers (ARBs) potentiate the reversion of adverse alterations of cardiac geometry and dysfunction via neurohormonal modulation and amelioration of remodeling, as relative to other available antihypertensive products.[14]

Remarkably, previous studies showed that the AT1 suppressor irbesartan exerts anti-hypertrophic effects, with markedly reduced normalized left/right ventricular weights, left ventricular end-diastolic pressure, and myocardial fibrotic area.[15,16] On top of that, although distinct populations have various prevalence rates of LVH and impaired LV geometry, investigation targeting differential impacts of known risk factors on impaired LV geometrical patterns in large population of Chinese hypertensives treated with ARBs is still lacking. Therefore, the aim of the present work was to assess the prevalence rates of LVH and LV geometric patterns in irbesartan-treated hypertensive individuals in southern China.

2 | MATERIALS AND METHODS

2.1 | Patients

The present community-based cross-sectional study was performed in Dongguan city, Guangdong Province of China, between October 2014 and September 2017. Totally 10,883 patients (6623 males and 4260 females) were initially enrolled consecutively, who received a self-administered questionnaire, with a response rate of 97.62%. Among the initially recruited subjects, 7664 were excluded for incomplete information, and 1038 were excluded according to exclusion criteria. Finally, 1181 (488 men and 693 women) subjects treated with irbesartan monotherapy at 150–300 mg/day for more than 3 months and a mean hypertensive history of 6 ± 3.2 years were enrolled, 84% of whom were thoroughly examined. The study flowchart is shown in Figure 1. There was no significant difference between those included and excluded in gender, age, SBP level, and hypertensive history (data not shown).

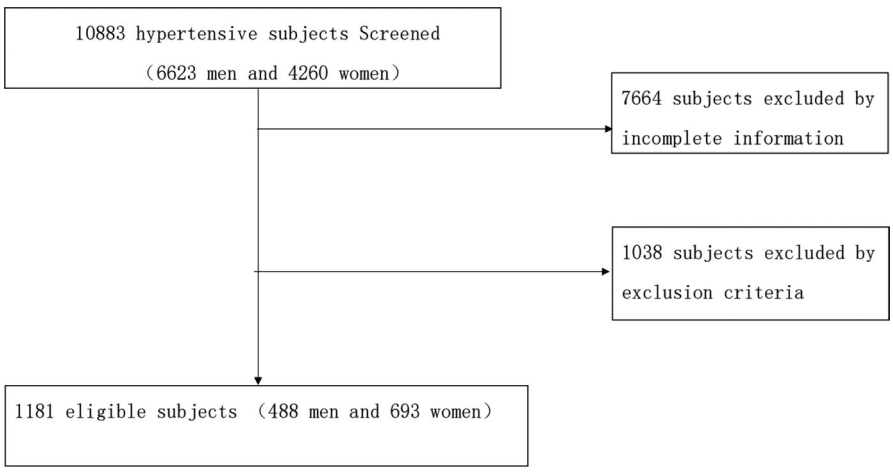

FIGURE 1 Flowchart

Hypertension was identified by seated systolic blood pressure (SBP) ≥140 mmHg, and/or diastolic blood pressure (DBP) ≥90 mmHg.

Inclusion criteria were as follows: (a) hypertension diagnosed by medical history and treatment with regular irbesartan monotherapy at 150–300 mg/day for more than 3 months; (b) age ranging from 40 to 80 years.

Exclusion criteria were as follows: secondary hypertension, severe ischemic heart disease, diabetic myocardiomyopathy, hypertrophic cardiomyopathy, congenital heart disease, significant valvular disease, severe arrhythmia, chronic renal dysfunction (serum creatine ≥ 442 mmol/L), malignant tumor, and autoimmune diseases. Additionally, to exclude irbesartan utilization for improving cardiac remodeling instead of antihypertension, individuals with heart failure and low ejection fraction (HFrEF, EF < 50%) were also excluded.

The present study abided by the 2007–2008 version of the Declaration of Helsinki. Informed consent was waived due to the retrospective design. The study protocol had approval from the ethics committee of Guangdong People's Hospital.

2.2 | Data collection

Eligible individuals, identified based on age and medical records, were invited to a community clinic by phone. For eligible individuals, study data were comprised of a self-administered questionnaire, anthropometric features, laboratory examinations, and echocardiographic data. The questionnaire encompassed demographic indexes, lifestyle, medical history, history of drugs, especially the duration and daily dose of irbesartan.

2.3 | Physical examination

Anthropometric data and blood pressure were measured by experienced research staff in the morning under standardized conditions as described previously. Trained nurses performed BP measurements in the sitting position with an automatic device (53000-E2, Welch Allyn) three times following a 5-min rest, with ≥30 s intervals between measurements. The second and third BP values were averaged and entered in the final BP analysis.

2.4 | Laboratory procedures

Venous blood samples were collected in the morning following overnight fasting. Laboratory procedures were performed under standardized conditions.

2.5 | Echocardiography

Echocardiographic measurements were performed by three skilled sonographers independently, based on routine protocols on an HP5500 (Phillips Medical System) per current guidelines.[17]

Parasternal long- and short-axis view images were assessed. The transducer's frequency ranged from 2.5 to 3.5 MHz. An Optigo echocardiographic recorder (Agilent) was used occasionally for screening a given patient unable to reach the local health center. Before the study, sonographers had specialized training in the echocardiography department of Guangdong Cardiovascular Institute.

2.5.1 | Parameter assessments

Left ventricular mass (LVM) was derived as follows:

$LVM = 0.8 \times 1.04 \times [(IVSd + LVIDD + PWTd)^3 - LVIDD^3] + 0.6$, yielding results tightly correlated with necropsy[18] ($R = 0.90$), in which IVSd and PWTd are septal and posterior wall thicknesses at the end of diastole, respectively; IVIDD represents left ventricular end-diastolic diameter.

LVM was divided by body surface (BSA) to calculate the LVM index (LVMI). BSA was obtained by the Du Bois formula as follows: $BSA = 0.0071\,843 \times (weight(kg))^{0.4253} \times (height(cm))^{0.725}$.[19] Increased LVMI was defined as LVMI exceeding 115 g/m^2 and 95 g/m^2 in men and women, respectively.[14] For further diagnosis of LVH and impaired geometric patterns, relative wall thickness (RWT) obtained as $2 \times PWTd/LVIDD$.[20]

LV geometry was grouped into 4 patterns according to LVMI and RWT[17]:

(a) normal geometry, normal LVMI and RWT < 0.42; (b) concentric remodeling, normal LVMI and RWT ≥ 0.42; (c) eccentric hypertrophy, increased LVMI and RWT < 0.42; concentric hypertrophy, increased LVMI and RWT ≥ 0.42.

2.6 | Statistical analysis

For continuous variables, data are presented as mean ± standard deviation (SD) and compared by the Student *t* test. Categorical variables were presented as frequency and assessed by the chi-square test. Statistical difference among multiple groups was evaluated by two-way analysis of variance (ANOVA). Logistic regression was applied to determine odds ratios (ORs), the corresponding 95% confidence intervals (CIs), and the increment of risk factors. Age, gender, height, weight, BMI, SBP, DBP, waistline, serum creatine, LDL-C, HDL-C, TG, TP, APO-A, APO-B, total cholesterol, fasting blood glucose (FBG), uric acid, microalbuminuria (MAU), microalbumin-Cr (MAU-Cr), globulin, waistline to hipline ratio (WtHR), hipline, neck-circumference, current cigarette smoking status, current drinking status and daily dose of irbesartan were included in univariate logistic regression analysis. Variables that showed significance in univariate analysis and/or with clinical implication, including BMI, FBG, MAU, daily dose of irbesartan, SBP, and WtHR, were further assessed by multivariable logistic regression analysis to identify risk factors for LVH and impaired geometric patterns. Considering the significant

TABLE 1 Clinical and Echocardiographic characteristics of the study subjects

Characteristic	Male (n = 488)	Female (n = 693)	Whole group (n = 1181)	χ^2/t	p
Age, years	62.5 ± 12.4	64.4 ± 10.2	63.6 ± 11.2	−2.705	0.007
Height, cm	163.4 ± 6.1	152.6 ± 5.0	157.1 ± 7.7	32.089	<0.001
Weight, kg	68.1 ± 10.9	60.5 ± 10.3	63.6 ± 11.2	12.258	<0.001
BMI, kg/m^2	25.4 ± 3.5	25.9 ± 3.9	25.7 ± 3.8	−2.213	0.027
SBP, mmHg	134.5 ± 16.6	135.4 ± 16.1	135.0 ± 16.3	−0.968	0.333
DBP, mmHg	83.9 ± 12.4	81.7 ± 9.3	82.6 ± 10.8	3.341	<0.001
Waistline	88.4 ± 9.9	87.2 ± 9.5	87.7 ± 9.7	2.138	0.033
Serum creatine	91.8 ± 27.3	69.0 ± 40.9	78.4 ± 37.6	11.491	<0.001
LDL-C, mmol/L	93.0 ± 25.8	98.0 ± 40.9	96.0 ± 35.6	−2.581	0.010
HDL-C, mmol/L	45.9 ± 14.2	51.8 ± 15.8	49.4 ± 15.4	−6.708	<0.001
Triglyceride, mmol/L	161.9 ± 145.4	157.5 ± 126.5	159.3 ± 134.6	0.54	0.589
Total protein, mmol/L	73.3 ± 5.1	74.9 ± 4.3	74.3 ± 4.7	−5.969	<0.001
APO-A, mmol/L	1.1 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	−8.724	<0.001
APO-B, mmol/L	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	−0.579	0.563
Total cholesterol, mmol/L	191.1 ± 43.5	207.0 ± 45.5	200.4 ± 45.3	−6.005	<0.001
FBG, mmol/L	5.2 ± 1.3	5.4 ± 1.6	5.3 ± 1.5	−2.559	0.011
Uric acid, mmol/L	440.1 ± 115.5	375.2 ± 99.3	402.0 ± 110.9	10.065	<0.001
MAU	55.7 ± 88.5	43.1 ± 78.9	48.3 ± 83.2	2.521	0.012
MAU-Cr	3.4 ± 6.5	2.6 ± 4.5	3.0 ± 5.4	2.36	0.019
Globulin	27.4 ± 4.2	28.8 ± 4.4	28.2 ± 4.4	−5.45	<0.001
WtHR	53.9 ± 5.8	57.2 ± 6.3	55.8 ± 6.3	−9.267	<0.001
Hipline, cm	94.1 ± 7.4	94.1 ± 7.7	94.1 ± 7.6	−0.083	0.934
Neck_Circumference, cm	36.4 ± 3.1	32.8 ± 2.8	34.2 ± 3.4	20.318	<0.001
PW, cm	10.2 ± 1.5	9.4 ± 1.2	9.7 ± 1.4	8.793	<0.001
IVS, cm	10.5 ± 1.6	9.8 ± 1.2	10.1 ± 1.4	8.382	<0.001
LVESD, cm	27.9 ± 4.1	27.2 ± 3.8	27.5 ± 3.9	2.906	0.004
LVESV, cm	30.3 ± 10.8	28.4 ± 9.7	29.2 ± 10.2	3.113	0.002
LVEDD, cm	46.3 ± 4.9	45.0 ± 4.6	45.5 ± 4.7	4.55	<0.001
LVEDV, cm	100.3 ± 24.8	93.9 ± 22.3	96.5 ± 23.6	4.541	<0.001
Diabetes mellitus	81 (16.7%)	150 (21.8%)	231 (19.7%)	4.661	0.031
Coronary heart disease	10 (2.1%)	14 (2.0%)	24 (2.0%)	0.001	0.973
Current Cigarette Smoking	226 (46.3%)	0 (0.0%)	226 (19.1%)	538.403	<0.001
Current Drinking	39 (9.4%)	1 (0.1%)	40 (3.6%)	182.568	<0.001
BSA	1.7 ± 0.2	1.6 ± 0.1	1.6 ± 0.2	19.275	<0.001
LVM	168.4 ± 43.1	146.4 ± 30.1	155.5 ± 37.6	9.771	<0.001
LVMI	97.6 ± 24.2	94.2 ± 19.2	95.6 ± 21.5	2.624	0.009
LVMI-height$^{2.7}$ (g/m$^{2.7}$)	26.2 ± 7.3	30.3 ± 7.2	28.6 ± 7.5	−9.708	<0.001
Daily dose of irbesartan (300 mg/day)	93 (19.1%)	129 (21.5%)	222 (20.4%)	0.989	0.320

Abbreviations: BMI, body mass index; BSA, body surface area; FBG, fasting blood glucose; IVS, Interventricular septal; LVEDD, Left ventricular end-diastolic volume; LVEDV, left ventricular end-diastolic volume; LVESD, left ventricular end-systolic diameter; LVESV, Left ventricular end-systolic volume; LVM, left ventricular mass; LVMI, left ventricular mass index; MAU, microalbuminuria; MAU-Cr, microalbuminuria to creatine ratio; PW, posterior wall; SBP, systolic blood pressure; WtHR, waistline to hipline ratio.

difference in baseline features between genders, the logistic regression model was applied in males and females, separately. Two-sided $p < 0.05$ indicated statistical significance. SAS 9.4 for Windows (release 6.11, USA) was utilized for statistical analysis. To evaluate the related increment of risk factors, percentage change (PC) was adopted.

3 | RESULTS

3.1 | Patient baseline and echocardiographic properties

Totally 1181 irbesartan-treated hypertensives (488 men and 693 females) with complete data were analyzed. The study flowchart is presented in Figure 1. The majority of clinical characteristics, including age, height, weight, BMI, DBP, waistline, serum creatine, LDL-C, HDL-C, total protein, Apo-A, total cholesterol, fasting blood glucose, uric acid, MAU, MAU-Cr, globulin, WtHR, and neck-circumference, differed significantly between genders. Details of baseline clinical and echocardiographic characteristics are presented in Table 1. Regarding echocardiographic data, LVEDD, PWTd, and LV mass were significantly higher in males as comparison with that in females (46.27 ± 4.86 vs 45.01 ± 4.58, 10.15 ± 1.49 vs 9.44 ± 1.21, and 168.42 ± 43.05 vs 146.35 ± 30.07, respectively; all $p < 0.001$). A similar trend was obtained for BSA (97.63 ± 24.20 vs 94.18 ± 19.22, $p = 0.009$). Meanwhile, RWT was slightly but not significantly higher in women compared with men.

3.2 | Prevalence of LVH in irbesartan-treated hypertensive population

Among the 1181 irbesartan-treated hypertensive patients, 21.5% of males ($n = 105$) and 44.1% of females ($n = 306$) showed LVH. The proportions of both concentric and eccentric hypertrophies increased with aging. Details of LV geometric pattern distribution are presented in Table 2.

3.3 | LV geometric pattern distribution and its associations with clinical characteristics

As shown in Table 2, the prevalence for normal geometry, concentric hypertrophy, eccentric hypertrophy, and concentric remodeling was 40.2%, 14.8%, 5.9%, and 39.1% among males, respectively; the corresponding values were 48.3%, 8.5%, 6.2%, and 36.9% for females, respectively. Moreover, the distribution of abnormal LV geometry had a positive correlation with aging (55.4%, 59.7%, and 65.9% in subjects aged < 45 years, 45–60 years, and ≥60 years, respectively, $p = 0.002$). Univariate analysis indicated that cigarette smoking ($\chi^2 = 38.965$, $p < 0.001$), current drinking ($\chi^2 = 34.928$, $p < 0.001$), daily dose of irbesartan ($\chi^2 = 9.413$, $p = 0.024$), BMI ($F = 3.004$, $p = 0.030$), HDL-C ($F = 3.250$, $p = 0.021$), apoprotein A ($F = 4.428$, $p = 0.004$), waist to height ratio ($F = 9.048$, $p < 0.001$), and neck-circumference ($F = 10.869$, $p < 0.001$) had significant associations with LV geometric pattern distribution. Besides, SBP and MAU-Cr were marginally associated with the distribution of LV geometric pattern ($p = 0.096$ and 0.097, respectively). Further, SBP and MAU showed an increasing trend, although not significant, across the concentric remodeling, eccentric hypertrophy and concentric hypertrophy groups (134.041 ± 16.147 mmHg, 136.515 ± 17.736 mmHg and 136.721 ± 16.032 mmHg for SBP, respectively; 50.285 ± 82.299 mg/day, 53.688 ± 91.291 mg/day and 54.673 ± 88.878 mg/day for MAU, respectively).

3.4 | Risk factors for LVH in irbesartan-treated hypertensive patients

Based on relevant findings from the analysis of clinical characteristics and LV geometric pattern distribution, BMI, FBG, daily dose of irbesartan, MAU, SBP, cigarette smoking and WtHR in males, and BMI, MAU-Cr, daily dose of irbesartan, MAU, SBP and WtHR in females were assessed by univariable and multivariable logistic regression analyses as potential risk factors for LVH.

Multivariable analysis after controlling for confounders revealed that WtHR was significantly associated with LVH in both males (OR = 1.10, 95% CI 1.04–1.16; $p = 0.001$) and females (OR = 1.06, 95% CI 1.02–1.10; $p = 0.004$). The abovementioned findings are detailed in Table 3.

3.5 | Risk factors for impaired LV geometric pattern in irbesartan-treated hypertensives

In multivariate analysis after adjusting for confounders, risk factors for concentric hypertrophy in males included SBP (OR = 1.02, 95% CI 1.00–1.04; $p = 0.024$) and WtHR (OR = 1.08, 95% CI 1.00–1.15; $p = 0.038$); in females, MAU-Cr (OR = 1.11, 95% CI 1.01–1.23; $p = 0.033$) and WtHR (OR = 1.08, 95% CI 1.03–1.13; $p = 0.002$) were risk factors. Risk factors for concentric remodeling in both genders included WtHR, with OR = 1.10 (95% CI 1.03–1.18; $p = 0.003$) in males and OR = 1.05 (95% CI 1.00–1.11; $p = 0.037$) in females. Further, risk factors for eccentric hypertrophy were FBG (OR = 1.39, 95% CI 1.02–1.91; $p = 0.039$) and WtHR (OR = 1.11, 95% CI 1.01–1.23; $p = 0.035$) in males. These findings are detailed in Table 4.

4 | DISCUSSION

LVH and impaired LV geometry are considered markers of subclinical cardiac damage, attributes not only to pressure overload but also to multiple factors, including overactivation of the RAAS. Furthermore, emerging evidence indicates that escalated plasma aldosterone levels are detected in the conditions of cardiovascular disease. For instance, aldosterone might be multifold higher in HF cases compared with healthy controls.[18] Indeed, blocking RAAS overactivation under pathological conditions may participate in ARB's beneficial effects on cardiovascular remodeling, as well as BP reduction. Nevertheless, target organ damage, including LVH and left ventricular geometric abnormalities, might be affected by disease-related risk factors in addition to BP increase and RAAS overactivation. To the best of our knowledge,

TABLE 2 The distribution of LV geometric patterns (univariate analysis)

Characteristic	normal [*n* (%)]	Concentric hypertrophy [*n* (%)]	Eccentric hypertrophy [*n* (%)]	Concentric remodeling [*n* (%)]	χ^2/F	*p*
Sex						
Male	206 (42.2)	75 (15.4)	30 (6.1)	177 (36.3)	73.771	<0.001
Female	224 (32.3)	165 (23.8)	141 (20.3)	163 (23.5)		
Age group (years)						
<45	29 (44.6)	6 (9.2)	6 (9.2)	24 (36.9)	20.598	0.002
45-60	131 (40.3)	55 (16.9)	36 (11.1)	103 (31.7)		
≥60	270 (34.1)	179 (22.6)	56 (16.3)	213 (26.9)		
Diabetes mellitus	85 (36.8%)	51 (22.1%)	32 (13.9%)	63 (27.3%)	0.875	0.831
Coronary heart disease	6 (25.0%)	3 (12.5%)	3 (12.5%)	12 (50.0%)	5.504	0.138
Cigarette Smoking						
Never Smokers	309 (34.6%)	195 (21.8%)	154 (17.2%)	236 (26.4%)	38.965	<0.001
Smokers	88 (38.9%)	39 (17.3%)	15 (6.6%)	84 (37.2%)		
Current Drinking						
Never	375 (37.5%)	168 (16.8%)	162 (16.2%)	295 (29.5%)	34.928	<0.001
Every Day	11 (57.9%)	0 (0.0%)	2 (10.5%)	6 (31.6%)		
Daily Dose of irbesartan						
300 mg/day	404 (36.6%)	225 (20.4%)	165 (14.9%)	311 (28.1%)	9.413	0.024
150 mg/day	20 (36.4%)	9 (16.4%)	2 (3.6%)	24 (43.6%)		
Height, cm	158.3 ± 7.9	155.5 ± 7.4	153.9 ± 6.5	158.2 ± 7.5	20.384	<0.001
Weight, kg	65.1 ± 11.4	61.9 ± 11.4	62.0 ± 10.8	63.8 ± 10.8	5.758	<0.001
BMI, kg/m^2	25.8 ± 3.9	25.6 ± 4.0	26.5 ± 3.8	25.4 ± 3.5	3.004	0.030
SBP, mmHg	134.2 ± 15.8	136.7 ± 16.0	136.5 ± 17.7	134.0 ± 16.1	2.116	0.096
DBP, mmHg	82.4 ± 9.9	82.5 ± 10.5	82.6 ± 13.5	82.947 ± 10.5	0.188	0.905
Waistline	87.6 ± 9.8	87.8 ± 10.4	87.8 ± 9.9	87.7 ± 9.1	0.040	0.990
Serum creatine	77.4 ± 25.2	80.2 ± 32.3	75.1 ± 37.1	80.1 ± 26.0	0.950	0.416
LDL-C, mmol/L	95.7 ± 26.2	100.3 ± 28.9	93.5 ± 26.3	94.5 ± 26.9	1.660	0.174
HDL-C, mmol/L	49.4 ± 16.7	50.2 ± 12.5	51.9 ± 21.8	47.6 ± 11.0	3.250	0.021
Triglyceride, mmol/L	160.4 ± 148.3	158.9 ± 125.2	156.4 ± 138.3	159.6 ± 120.7	0.038	0.990
Total protein, mmol/L	74.4 ± 5.4	74.5 ± 4.3	73.9 ± 4.1	74.1 ± 4.3	0.726	0.537
APO-A, mmol/L	1.2 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	4.428	0.004
APO-B, mmol/L	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	1.1 ± 0.2	0.314	0.815
Total cholesterol, mmol/L	202.5 ± 46.4	202.4 ± 40.8	201.3 ± 43.0	196.0 ± 48.0	1.552	0.199
FBG, mmol/L	5.2 ± 1.5	5.3 ± 1.3	5.2 ± 1.3	5.3 ± 1.6	0.424	0.736
Uric acid, mmol/L	402.7 ± 113.7	406.1 ± 106.9	383.9 ± 101.8	407.5 ± 114.2	1.909	0.126
MAU	41.1 ± 26.8	54.7 ± 38.9	53.7 ± 31.3	50.3 ± 32.3	1.856	0.135
MAU-Cr	2.5 ± 1.8	3.6 ± 17.0	3.0 ± 1.7	3.0 ± 1.8	2.110	0.097
Globulin	28.2 ± 4.8	28.6 ± 4.6	27.7 ± 3.8	28.4 ± 3.9	1.407	0.239
WtHR	54.9 ± 6.4	56.7 ± 6.7	57.5 ± 5.9	55.5 ± 5.8	9.048	<0.001
Hipline, cm	94.5 ± 7.7	93.6 ± 7.7	93.9 ± 7.8	94.1 ± 7.3	0.668	0.572
Neck_Circumference, cm	34.5 ± 3.4	33.9 ± 3.5	33.0 ± 3.1	34.7 ± 3.5	10.869	<0.001
Total	430 (36.4%)	240 (20.3%)	171 (14.5%)	340 (28.8%)		

TABLE 3 Univariate and multivariable logistic regression analyses of risk factors for LVH

	Univariate analysis			Multivariable analysis		
Effect	**OR[a]**	**OR 95% CI**	***p* value**	**OR**	**OR 95% CI**	***p* value**
Male						
BMI, kg/m^2	1.01	0.96–1.06	0.766	0.90	0.82–0.98	0.019
FBG, mmol/L	1.15	0.98–1.34	0.088	1.12	0.95–1.32	0.195
Daily Dose of irbesartan (300 mg/day vs 150 mg/day)	0.89	0.36–2.19	0.798	0.98	0.38–2.52	0.965
MAU, mmol/L	1.00	1.00–1.00	0.059	1.00	1.00–1.00	0.199
SBP, mmHg	1.01	1.00–1.02	0.089	1.01	1.00–1.02	0.084
Cigarette Smoking: Former Smokers vs Never Smokers	0.62	0.35–1.11	0.106	0.63	0.35–1.13	0.121
Cigarette Smoking: Smokers vs Never Smokers	1.15	0.78–1.69	0.482	1.12	0.75–1.67	0.572
whtr	1.05	1.01–1.08	0.007	1.10	1.04–1.16	0.001
Female						
BMI, kg/m^2	0.98	0.95–1.03	0.448	0.93	0.88–0.99	0.020
MAU_Cr[b]	1.04	1.00–1.09	0.042	1.03	0.97–1.10	0.268
Daily Dose of irbesartan (300 mg/day vs 150 mg/day)	1.05	0.51–2.19	0.891	1.03	0.49–2.18	0.934
MAU, mmol/L	1.00	1.00–1.00	0.097	1.00	1.00–1.00	0.770
SBP, mmHg	1.00	0.99–1.01	0.988	1.00	0.99–1.01	0.618
whtr[c]	1.02	1.00–1.05	0.114	1.06	1.02–1.10	0.004

[a]OR: The predicted value of the odd ratio (OR) for every one unit change in the effect variable.

[b]Microalbuminuria (mmol/L) to creatine (mmol/L) ratio.

[c]Waistline (cm) to hipline (cm) ratio.

however, little information is available on the prevalence of and risk factors for impaired left ventricular geometrical patterns in ARB-treated hypertensive individuals. Therefore, the present study raised tested the hypothesis that LVH and left ventricular geometric abnormalities under the setting of hypertension are not only a consequence of hypertension but also represent a pathological process simultaneously progressing with hypertension. The present study revealed that the prevalence of LVH among irbesartan-treated community hypertensive individuals were 20.7% and 14.7% for male and female, respectively. In previous reports, LVH prevalence varied from 19% to 48% in untreated hypertensive cohorts,[19,20] whereas impaired LV geometric pattern was shown to be 39.1%, 14.8%, and 5.9% for the concentric remodeling, concentric hypertrophy, and eccentric hypertrophy groups in males, respectively, and 36.9%, 8.5%, and 6.2% in females, accordingly. As anticipated, concentric remodeling was the most prevalent LV geometry impairment in both genders.

Similarly, the Atherosclerosis Risk in Community (ARIC) discovered a prevalence of approximately 65% of in concentric hypertrophy or concentric remodeling across hypertensive individuals.[21] Concentric hypertrophy, which is associated with worse cardiovascular prognosis,[22] was far less frequent than concentric remodeling, but more prevalent as compared with eccentric hypertrophy in this study. The present data contrasted findings in mostly white elderly individuals of the Cardiovascular Health Study, which revealed that eccentric hypertrophy (2.2%) was more abundant than concentric hypertrophy (0.6%), upon controlling for heart failure, coronary heart disease, valvular cardiomyopathy, arterial fibrillation, and stroke.[23] The abovementioned inconsistency might be explained by differences in age, gender, hypertension history, duration of irbesartan administration, geographical region, and other risk factors. Further, in the Losartan Intervention For Endpoint reduction in hypertension (LIFE) trial, losartan administration resulted in conversion from concentric hypertrophy to eccentric hypertrophy in 34% of hypertensives with baseline concentric hypertrophy, while only 3% showed conversion from eccentric hypertrophy to concentric hypertrophy.[24] Additionally, population-based studies evaluating hypertensive individuals indicated that LVM after normalization to BSA detects less LVH cases in comparison with that to height to allometric signals.[25,26] Consistently, a meta-analysis of 2213 treated hypertensives suggested that LVH derived from left ventricular/BSA demonstrated lower prevalence compared with that calculated as LVM/h$^{2.7}$ (31% vs 46%).[27]

Moreover, we found that WtHR was significantly associated with concentric hypertrophy, eccentric hypertrophy, and remodeling after adjustment for other risk factors in both males and females, indicating that additional measurement of WtHR may prove beneficial in further assessing hypertensive adults for metabolic

TABLE 4 The multivariable logistic regression analyses of risk factors for abnormal geometric patterns

	Concentric hypertrophy			Eccentric hypertrophy			Concentric remodeling		
Effect	**OR[a]**	**OR 95% CI**	***p* value**	**OR**	**OR 95% CI**	***p* value**	**OR**	**OR 95% CI**	***p* value**
Male									
BMI, kg/m^2	0.93	0.83–1.04	0.203	0.89	0.76–1.04	0.147	0.89	0.80–0.98	0.022
FBG, mmol/L	1.06	0.81–1.40	0.661	1.39	1.02–1.91	0.039	1.11	0.93–1.33	0.255
Daily Dose of irbesartan (300 mg/day vs 150 mg/day)	0.25	0.03–2.34	0.223	0.00	0.00–I	0.978	1.39	0.53–3.63	0.500
MAU, mmol/L	1.00	1.00–1.01	0.066	1.00	1.00–1.01	0.103	1.00	1.00–1.00	0.635
SBP, mmHg	1.02	1.00–1.04	0.024	1.02	1.00–1.04	0.087	1.00	0.99–1.02	0.496
Cigarette Smoking: Former Smokers vs Never Smokers	0.45	0.16–1.22	0.116	0.41	0.08–2.00	0.270	0.69	0.36–1.33	0.272
Cigarette Smoking: Smokers vs Never Smokers	1.26	0.70–2.28	0.440	1.33	0.55–3.21	0.521	1.05	0.67–1.63	0.846
whtr	1.08	1.00–1.15	0.038	1.11	1.01–1.23	0.035	1.10	1.03–1.18	0.003
Female									
BMI, kg/m^2	0.87	0.81–0.95	0.001	1.01	0.93–1.10	0.745	0.91	0.84–0.98	0.017
MAU_Cr[b]	1.11	1.01–1.23	0.033	1.01	0.94–1.08	0.800	1.03	0.95–1.12	0.465
Daily Dose of irbesartan (300 mg/day vs 150 mg/day)	0.98	0.37–2.59	0.973	0.33	0.07–1.55	0.161	1.60	0.69–3.69	0.275
MAU, mmol/L	1.00	0.99–1.00	0.184	1.00	1.00–1.01	0.383	1.00	1.00–1.01	0.702
SBP, mmHg	1.00	0.98–1.01	0.859	1.00	0.99–1.01	0.910	0.99	0.98–1.01	0.289
whtr[c]	1.08	1.03–1.13	0.002	1.04	0.98–1.10	0.160	1.05	1.00–1.11	0.037

[a]OR: The predicted value of the odd ratio (OR) for every one unit change in the effect variable.

[b]Microalbuminuria (mmol/L) to creatine (mmol/L) ratio.

[c]Waistline (cm) to hipline (cm) ratio.

disturbances and cardiovascular complications after treatment with ARB drugs. Overall, confirming WtHR as an independent risk factor for LV hypertrophy and geometric abnormality by the present study has a crucial implication for future investigations targeting WtHR to alleviate LV remodeling in irbesartan-treated hypertensives.

BP is considered an important pathological factor for LV geometry alteration. Logistic regression analysis suggested a positive correlation between 1-mmHg elevation in systolic or diastolic BP and a 2%–4% increase in the odds of impaired LV dimensional indices.[28-33] With a followed up of 132 normotensives for 4.7 years, De Simone et al demonstrated that LVM is significantly greater in individuals who developed hypertension (11%) relative to those who remained normotensive.[34] Similarly, in the present study, SBP had an increasing trend across the concentric remodeling, eccentric hypertrophy, and concentric hypertrophy groups; notably, SBP was significantly elevated in males with concentric hypertrophy.

As shown in the present study, MAU progressively escalated across the concentric remodeling, eccentric hypertrophy, and concentric hypertrophy groups, corroborating another study in which MAU seemed to have significant effects on abnormal LV geometry and higher LV mass in diabetic patients with ECG LV hypertrophy.[35] Besides, MAU was marginally associated with concentric hypertrophy in males. Furthermore, although not significantly, MAU-Cr was moderately associated with the distribution of LV geometric patterns; notably, MAU-Cr was remarkably correlated with concentric hypertrophy in females. Taken together, the current findings indicated a potential link between cardiac damage and microvascular abnormalities in our target population.

Importantly, the present study disclosed that the daily irbesartan dose was markedly associated with the distribution of LV geometric patterns, thus providing a rationale for further utilization of irbesartan in the prevention of LV hypertrophy and geometric abnormalities.

Nevertheless, the present report demonstrated that BMI was significantly lower in LV concentric hypertrophy and concentric remodeling in both genders, which contradicted the previous cross-sectional studies indicating that BMI is positively related to eccentric and concentric LVH geometric patterns.[36,37] This discrepancy was probably due to small sample size and the involvement of other metabolic risk factors.

As a retrospective community-based study, the present work revealed the prevalence of and risk factors for impaired left ventricular geometrical patterns in hypertensive individuals with administration of irbesartan, highlighting a high prevalence of LVH and abnormal geometry among such population, further indicating the intensive management of relative risk factors as an important therapeutic goal for preventing cardiac damage in these irbesartan-treated hypertensives.

4.1 | Study limitations

The cross-sectional design does not allow strong causal inferences, thus limiting the prediction of cardiovascular and cerebrovascular events in abnormal LV geometric patterns, which deserves further investigation by prospective studies. Although this study had a larger cohort sample in comparison with previous ones targeting hypertensive populations by echocardiography, the possibility of its power being too low to disclose risk factors significantly associated with abnormal LV geometric patterns cannot be excluded. Furthermore, our findings cannot be fully applied across Han Chinese individuals, as the subjects assessed in the current study comprised irbesartan-treated hypertensives only from Guangdong Province of China.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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