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Sex-Specific Association of Left Ventricular Hypertrophy With Cardiovascular Events in High-Risk of Cardiovascular Disease Population: Findings From the Sub-Cohort of China PEACE Million Persons Project

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ABSTRACT

Sex differences significantly influence the prognosis of left ventricular hypertrophy (LVH). To investigate sex-specific differences in the incidence of major adverse cardiovascular event (MACE) among individuals with LVH, we enrolled 14 636 (mean age 57 years, women 59.1%) participants with high risk for cardiovascular diseases (CVD) from the sub-cohort of the China PEACE Million Persons Project. LVH was identified by echocardiography dividing left ventricular mass (LVM) by body surface area (BSA), height$^{1.7}$, or height$^{2.7}$ using validated sex-specific cutoff values. MACE was defined as a composite of coronary heart disease, myocardial infarction, strokes, heart failure, and/or cardiovascular death. During a median follow-up of 3.62 years, 1327 patients developed MACE. The prevalence of LVH was higher when indexing LVM to BSA and height$^{1.7}$ in women. Higher blood pressure (BP) and previous diabetes mellitus (DM) were associated with a higher risk of LVH in both genders, while aging and adiposity had a more hazardous impact in women than in men. Multivariable Cox regression analyses indicated an increasing risk between LVH and MACE exclusively in men. In individuals diagnosed with LVH, women exhibited a reduced risk for MACE. When indexing LVM to BSA, concentric hypertrophy (adjusted hazard ratio [aHR]: 1.73, 95% CI: 1.37–2.19; $p < 0.001$] and eccentric hypertrophy (aHR: 1.54, 95% CI: 1.06–2.25; $p = 0.025$) were significantly associated with MACE in men. In this population study, risk factors including BP, blood glucose, lipids level, and BMI should be managed strictly. Additionally, men should pay more attention to the occurrence of LVH, which had a greater association with MACE.

Shiping Wu and Xiaoxuan Feng are co-authors and they contributed equally to this work.

1 | Introduction

Left ventricular hypertrophy (LVH) is a response to various pathophysiological stimuli that closely follow the progression of the disease and provide useful predictive information regarding clinical outcomes [1]. The evaluation of LVH utilizes different body size indicators to standardize left ventricular mass (LVM) and obtain diagnostic criteria based on sex [2]. LVM can be readily assessed through diverse non-invasive methodologies, with echocardiography being the most pivotal. Cardiovascular (CV) risk factors, such as age, sex, smoking, hypertension (HTN), diabetes mellitus (DM), dyslipidemia, and previous history of cardiovascular disease (CVD), can lead to LVH by increasing a load of left heart pressure and volume as an adaptive response, which researchers have extensively ascertained [1, 3–7]. In addition to connecting several CVD risk factors, the primary benefit of assessing LVH is its significance in predicting clinical outcomes [1]. Initial results from the Framingham Heart study, which included echocardiographic data, showed that baseline LVM was a strong predictor of developing CVD, death from CVD, and all-cause mortality [8]. Previous studies also pointed out that patients with concentric hypertrophy were found to have the highest all-cause as well as cardiovascular mortality rate compared with other geometric patterns [9, 10].

Biological sex is a crucial determinant that might impact the prevalence, risk factors, and prognostic value of LVH and its geometric patterns. The Campania Salute Network study [11] found that obesity and DM were associated with an increased risk of LVH in women, with LVH being more prevalent in hypertensive women than in men. Among hypertensive patients with LVH, the risk of major adverse cardiovascular events (MACE) is similar for both women and men. Additionally, in patients with known or suspected coronary artery disease undergoing cardiovascular magnetic resonance (CMR), concentric remodeling was more prevalent in women and associated with increased all-cause mortality in both sexes, whereas eccentric hypertrophy conferred this risk only in women [4]. In summary, prior studies have shown the need to clarify the differences between sexes in terms of the characteristics and geometric patterns of LVH, as well as its risk factors and prognostic values.

Therefore, our study aimed to evaluate the sex-specific differences prevalence and risk factors of LVH in patients with high risk of CVD and further investigated the differences in the prognostic value of LVH in women and men.

2 | Methods

2.1 | Study Population

The China Patient-centered Evaluative Assessment of Cardiac Events (PEACE) Million Persons Project (MPP) is a nationwide and government-funded study identifying individuals at high risk for CVD through population-based screening. The details of the design and methodology of PEACE MPP have been described elsewhere [12, 13]. The current study data were applied from the Early Screening and Comprehensive Intervention Program for High-Risk Population of CVD, which is an essential part of PEACE MPP (Trial Registration Number NCT02536456). Participants are considered at high risk of CVD if they meet at least one of four criteria adapted from WHO guidelines: (1) established CVD; (2) systolic blood pressure (SBP) ≥ 160 mm Hg or diastolic blood pressure (DBP) ≥ 100 mm Hg; (3) dyslipidemia; and (4) 10 years CVD risk ≥20% [14]. CVD was defined as having coronary heart disease (CHD) or having a history of myocardial infarction (MI) or stroke.

The current study was conducted in a sub-cohort of the PEACE MPP in southern China that recruited 28 578 community-dwelling adults in high risk from eight sites across Guangdong Province. After excluding the participants with missing echocardiographic parameters, including relative wall thickness (RWT) (n = 9739) and LVM (n = 4), and missing clinical characteristics, including height (n = 10) and physical activity (n = 2850), 15 977 participants with complete baseline data remained. We further excluded the individuals with previous heart failure (HF), stroke, CHD, MI, cancer, chronic kidney disease, moderate or greater valve regurgitation or valve stenosis, and a history of valve replacement surgery (n = 1341). Finally, 14 636 participants were included (Figure S1).

2.2 | Clinical Characteristics Collections

We applied standardized questionnaires to assess sociodemographic information (such as age and sex), lifestyle behaviors (such as smoking, alcohol drinking history, and physical activity), socioeconomic status (including educational status, occupation, residence, family annual income, marriage, and insurance), previous disease history (including HTN, DM, dyslipidemia, HF, stroke, CHD, MI, cancer, chronic kidney disease, and valve replacement surgery), and medication history (including anti-hypertensive, glycemic, and dyslipidemia treatment) of the participants. Body mass index (BMI) was calculated by body mass (kg) divided by the square of height (m^2). Overweight and obesity were defined as BMI 24–27.9 kg/m^2 and ≥28 kg/m^2, respectively. Blood pressure (BP) measurements were conducted on the right upper arm twice following a 5 min rest period in a seated position, using an electronic BP monitor (Omron HEM-7430; Omron Corporation, Kyoto, Japan), and the average value was recorded [15]. Blood samples were collected in a fasting state to test the blood glucose and lipid profile. Low-density lipoprotein cholesterol (LDL-C) was calculated by Friedewald formula using the values of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG). HTN was defined as examined SBP ≥ 140 mm Hg or/and DBP≥ 90 mm Hg, current antihypertensive medication, or self-reported. Diabetes was defined as fasting blood glucose (FBG) ≥ 7.0 mmol/L, current glycemic treatment, or self-reported. Dyslipidemia was defined as using lipid-lowering drugs, self-reported TC, LDL-C, TG increased or HDL-C decreased, TC < 5.2 mmol/L and TG < 1.7 mmol/L were appropriate levels.

2.3 | Echocardiographic Parameters

The echocardiography examinations were conducted by sonographers from Guangdong Provincial People's Hospital and local ultrasound doctors, adhering to the protocol set by the National Health and Family Planning Commission of China, as detailed

in previous reports [12]. Echocardiographic parameters included inter-ventricular septal dimension at end-diastole (IVSd), posterior wall thickness at end-diastole (PWTd), and left ventricular end-diastolic diameter (LVEDd), which were obtained from 2D-guided linear measurements. Left ventricular ejection fraction (LVEF) was calculated from Teichholz's formula. Transmitral Doppler was utilized to obtain the peak early (E) and late (A) diastolic mitral annular velocities, and then we obtained E/A ratio. RWT was calculated according to the formula: $2 \times$ PWTd/LVEDd; LVM was calculated according to the Devereux formula: 0.8 (1.04 [IVSd + LVEDd + PWTd] [3] − (LVEDd) [3]) + 0.6 g. According to the ASE/EACVI and ESC/ESH guidelines [2], indexed LVM to body surface area (BSA) (LVM/BSA), the upper normal limit or threshold for LVM index (LVMi) was >115 g/m^2 in men and >95 g/m^2 in women, and when indexed LVM to height$^{2.7}$ (LVM/H$^{2.7}$), the threshold for LVMi was >50 g/H$^{2.7}$ in men and >47 g/H$^{2.7}$ in women. According to Chirinos et al. [16], when LVM indexed to height$^{1.7}$ (LVM/H$^{1.7}$), the threshold for LVMi was >81 g/H$^{1.7}$ in men and >60 g/H$^{1.7}$ in women. LV geometry was classified as follows: normal (normal LVMi and RWT), concentric remodeling (normal LVMi, increased RWT), eccentric hypertrophy (increased LVMi, normal RWT), and concentric hypertrophy (increased LVMi, increased RWT). LVH thresholds are shown in Table S4.

2.4 | Outcome Definition

MACE was defined as CHD, MI, stroke, HF, and/or cardiovascular death. We ascertained the outcomes through study investigators who were blinded to the other information reviewed and identified them by using ICD-10 (international classification of diseases, 10th revision) codes to identify the hospitalization records related to CHD (I20–I25), AMI(I21), HF(I50), stroke, and death from cardiovascular causes (I61–I64) from the Inpatients Registry. More precisely, CHD or MI was determined by the presence of chest pain or dyspnea, electrocardiographic changes, imaging evidence of coronary artery stenosis (≥50%), and/or elevated serum cardiac troponin levels. Stroke was identified through neurological impairments, such as abnormal reflexes and speech difficulties, and imaging-confirmed cerebrovascular occlusion. HF was determined based on the presence of clinical symptoms, including dyspnea or peripheral edema, along with structural or functional cardiac abnormalities identified by echocardiography and elevated natriuretic peptide levels. The HF outcome was ascertained through medical record review conducted via the Health Commission of Guangdong Province, with confirmation by local hospital experts and supporting evidence of impaired left ventricular function [17]. Mortality events were classified as CV deaths if directly linked to CV or cerebrovascular disease and otherwise as non-CV deaths.

2.5 | Statistical Analysis

Categorical variables were represented through the use of frequencies and percentages. The normality distribution of continuous data was assessed using the Kolmogorov–Smirnov test. Continuous variables were shown as mean ± standard deviation (SD) when normally distributed and as median with interquartile range (IQR) otherwise. Baseline characteristics among groups were compared by Chi-square test, one-way ANOVA, or Kruskal–Wallis H-test, depending on the appropriateness of each test. The missing values of LVEF ($n = 19$) and E/A ratio ($n = 682$) were filled with the critical intermediate value. Prior to the analysis, a collinearity test of the variables was conducted, and the variance inflation factor (VIF) was less than 5. Multivariable Logistic regression analyses were conducted separately for each sex to calculate the odds ratio (OR) and 95% confidence intervals (CI) with adjustment for covariates including age, SBP, DBP, heart rate (HR), BMI, current smoker, current drinker, education status, occupation, residence, family annual income, marriage, insurance, physical exercise, FBG, TG, LDL-C, TC, HDL-C, treatment (antihypertensive treatment, glycemic treatment, dyslipidemia treatment), HTN, DM, and dyslipidemia. The interactions between sexes and each covariate were examined using the interaction terms and the likelihood ratio tests. Kaplan–Meier curves and the Log-rank test to perform survival analysis for participants with and without LVH grouped by sex. Multivariable Cox regression analysis adjusted for covariates, as mentioned above, was conducted to estimate hazard ratio (HR) with 95% CI of LVH in predicting MACE and the role of sex in MACE in the presence or absence of LVH. Additionally, a sensitivity analysis was conducted using the Chinese thresholds for LVH proposed by Zhang et al. [18]. We re-assessed the association between sex, LVH patterns, and the risk of MACE through multivariable Cox regression. The adjustment variable of BMI was not included while indexing LVM to BSA; however, BMI was included as the adjustment variable when indexing LVM to H$^{1.7}$ or H$^{2.7}$. All analyses were conducted using RStudio version 4.3.1, SPSS version 26.0, and GraphPad Prism 8.0. $p < 0.05$ was regarded as statistically significant.

3 | Results

3.1 | Baseline Clinical and Echocardiographic Characteristics

Baseline characteristics of the study population are summarized in Table 1. The cohort's median age was 57.0 years (IQR 49.0–64.0 years), with 8650 (59.1%) women included. Women showed a lower median BMI (24.27 vs. 25.01 kg/m^2, $p < 0.001$) and were less likely to have overweight and obesity. Men were more likely to be current smokers and drinkers. Men exhibited higher SBP (137.5 vs. 140.5 mm Hg, $p < 0.001$) and DBP, higher TG but lower TC, LDL-C, and HDL-C than women. Women had a lower prevalence of HTN and DM while demonstrating a higher prevalence of dyslipidemia. Regarding socioeconomic status, women displayed lower educational status, lower family annual income, and higher farmer employment rates. In addition, it was observed that the percentage of women engaging in physical exercise almost daily was higher than that of men.

Sex-specific echocardiographic parameters at baseline are shown in Table 2. Women had a smaller IVSd, PWd, RWT, LVM, and LVMi but higher LVEF and E/A than men. Nevertheless, when LVM was indexed to BSA, the prevalence of eccentric and concentric hypertrophy was higher among women than men (Figure 1A). Although women had a higher prevalence of LVH, no significant sex difference in LVH geometric

TABLE 1 | Baseline clinical characteristics comparisons between men and women.

Variables	Women ($N = 8650$)	Men ($N = 5986$)	p value
Age (years)	57 (50–64)	56 (48–64)	<0.001
35–44	997 (11.5)	990 (16.5)	
45–54	2557 (29.6)	1718 (28.7)	
55–64	3222 (37.2)	1865 (31.1)	
65–75	1875 (21.7)	1415 (23.6)	
BMI (kg/m^2)	24.27 (22.21–26.67)	25.01 (22.96–27.11)	<0.001
Normal	4004 (46.3)	2202 (36.8)	
Overweight (24–28)	3323 (38.4)	2736 (45.7)	
Obesity (≥28)	1324 (15.3)	1050 (17.5)	
Height (cm)	154.5 (150.5–158.0)	166.0 (162.0–170.0)	<0.001
SBP (mm Hg)	137.5 (120.5–161.0)	140.5 (124.5–161.0)	<0.001
DBP (mm Hg)	80.0 (72.0–90.0)	85.5 (76.5–96.5)	<0.001
HR (bpm)	77.5 (71.0–85.0)	77.0 (71.0–84.9)	0.199
Current smoker, *n* (%)	68 (0.8)	2632 (44.0)	<0.001
Current drinker, *n* (%)	103 (1.2)	792 (13.2)	<0.001
Educational status (high school or above), *n* (%)	2089 (24.1)	2313 (38.6)	<0.001
Residence (urban), *n* (%)	3210 (37.1)	2317 (38.7)	0.051
Occupation (farmer), n (%)	691 (8.0)	391 (6.5)	0.001
Family annual income (50 000 yuan or above), no (%)	4160 (48.1)	3162 (52.8)	<0.001
Insurance, *n* (%)	8200 (94.8)	5710 (95.4)	0.119
Marriage (married), *n* (%)	7646 (88.4)	5664 (94.6)	<0.001
Physical exercise, *n* (%)			<0.001
Never	3437 (39.7)	2469 (41.2)	
Once in a while	659 (7.6)	635 (9.0)	
More than once a week	1628 (18.8)	1195 (20.0)	
Almost every day	2927 (33.8)	1788 (29.9)	
Hypertension, *n* (%)	4809 (55.6)	3893(63.3)	<0.001
Diabetes mellitus, *n* (%)	1615 (18.7)	1278 (21.3)	<0.001
Dyslipidemia, *n* (%)	4337 (50.1)	1876 (31.3)	<0.001
FBG (mmol/L)	5.70 (5.20-6.50)	5.70 (5.20-6.60)	0.046
TG (mmol/L)	1.51 (1.11-2.14)	1.61 (1.13-2.40)	<0.001
TC (mmol/L)	5.84 (4.74-6.88)	4.87 (3.95-6.02)	<0.001
LDL-C (mmol/L)	3.55 (2.30-4.46)	2.79 (2.04-4.00)	<0.001
HDL-C (mmol/L)	1.55 (1.26-1.89)	1.20 (0.96-1.48)	<0.001
Anti-hypertensive treatment, *n* (%)	2395 (27.7)	1763 (29.4)	0.02
Glycemic treatment, *n* (%)	630 (7.3)	581 (9.7)	<0.001
Dyslipidemia treatment, *n* (%)	444 (5.1)	359 (6.0)	0.024

Note: Data are median (interquartile range) or number (proportion).

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol.; HR, heart rate; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

patterns was observed when LVM indexed to $H^{1.7}$ (Figure 1B). Gender differences across LVH geometric patterns were only borderline statistically significant when LVM indexed to $H^{2.7}$ (Figure 1C).

3.2 | Risk Factors for LVH in Women and Men

Regardless of the method to define LVH, SBP ≥ 140 mm Hg and antihypertensive treatment were consistent risk factors for

TABLE 2 | Baseline echocardiographic parameters comparisons between men and women.

Variables	Women ($N = 8650$)	Men ($N = 5986$)	p value
IVSd (mm)	9.0 (8.5–10.0)	10.0 (9.0–11.0)	<0.001
PWd (mm)	9.0 (8.0–10.0)	10.0 (9.0–10.1)	<0.001
RWT	0.41 (0.37–0.45)	0.42 (0.38–0.46)	<0.001
LVM (g)	128.02 (109.83–152.95)	153.27 (132.32–181.22)	<0.001
LVEF (%)	69.0 (65.0–73.0)	68.0 (64.0–72.0)	<0.001
E/A	0.89 (0.74–1.22)	0.88 (0.73–1.22)	0.010
LVMi (LVM/BSA, g/m^2)	84.70 (72.98–97.66)	88.34 (76.80–101.90)	<0.001
LVH (LVM/BSA), *n* (%)	4745 (54.9)	3099 (51.8)	<0.001
LVMi (LVM/H$^{1.7}$, g/m^2)	62.01 (52.80–72.55)	65.18 (55.67–75.85)	<0.001
LVH (LVM/H$^{1.7}$), *n* (%)	6100 (70.5)	3239 (54.1)	<0.001
LVMi (LVM/H$^{2.7}$, g/m^2)	40.19 (34.00–47.46)	39.22 (33.49–45.65)	<0.001
LVH (LVM/H$^{2.7}$), *n* (%)	4565 (52.8)	3203 (53.5)	0.390

Note: Data are median (interquartile range) or number (proportion).

Abbreviations: A, peak late diastolic mitral annular velocities; BSA, body surface area; E, peak early diastolic mitral annular velocities; H, height; IVSd interventricular septal dimension at end-diastole; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; LVMi, left ventricular mass index; PWd, posterior wall thickness at end-diastole; RWT, relative wall thickness.

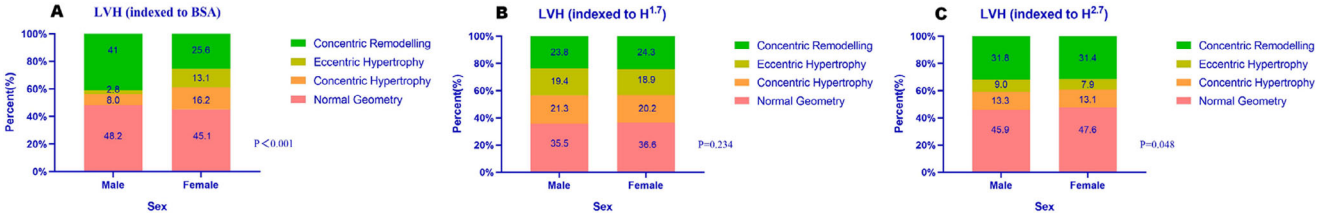

FIGURE 1 | Sex-specific prevalence of LV remodeling at baseline. (A) for the association between sex and LVH indexed to BSA. (B) for the association between sex and LVH indexed to H$^{1.7}$. (C) for the association between sex and LVH indexed to H$^{2.7}$. $p < 0.05$ is considered statistically significant. BSA, body surface area; H, height; LVH, left ventricular hypertrophy.

both men and women (all $p < 0.05$). As age increased, the risk of developing LVH rose for both sexes. A significant interaction between age and sex was observed (all p for interaction <0.001), indicating that the risk of LVH in women was higher than in men. High BP (SBP ≥ 140 mm Hg) was identified as a risk factor for LVH in both sexes. The study identified that elevated SBP levels ranging from 120 to 139 mm Hg, as well as abnormal DBP levels, were associated with an increased risk of LVH in women. Antihypertensive treatment was also significantly associated with LVH in both sexes (Table S1).

When LVM was indexed to BSA, TG ≥ 2.26 mmol/L and TC ≥ 6.22 mmol/L were significantly associated with LVH in both sexes. However, when LVM indexed to H$^{1.7}$ and H$^{2.7}$, TG ≥ 2.26 mmol/L was significantly associated with LVH only in women. DM, overweight, and obesity were identified as risk factors for LVH when LVM indexed to H$^{1.7}$ and H$^{2.7}$ in both sexes. Besides, overweight and obese significantly promoted higher risks of LVH in women compared to men (all p for interaction < 0.05). Among individuals with obesity, women exhibited a two-fold higher risk of developing LVH compared with men when LVM was indexed to H$^{1.7}$ (Table S1).

3.3 | CV Prognosis and LVH in Women and Men

Over a median follow-up of 3.62 years, a total of 1327 patients developed MACE, including 568 CHD, 89 MI, 762 strokes, 274 HF, and 68 cardiovascular deaths. The incident rate of MACE was significantly higher in men than women (11.2% vs. 7.6%, $p < 0.001$). Kaplan–Meier survival curves demonstrated that, regardless of the method used to define LVH, men had a higher risk of MACE than women. Furthermore, Kaplan–Meier survival curves indicated that individuals with LVH had a higher risk of MACE than those without LVH, irrespective of sex (Figure 2).

The multivariable-adjusted Cox regression analysis indicated that, irrespective of the definition of LVH employed, LVH was independently correlated with MACE in men, whereas no significant association was found in women (Table 3). Among patients

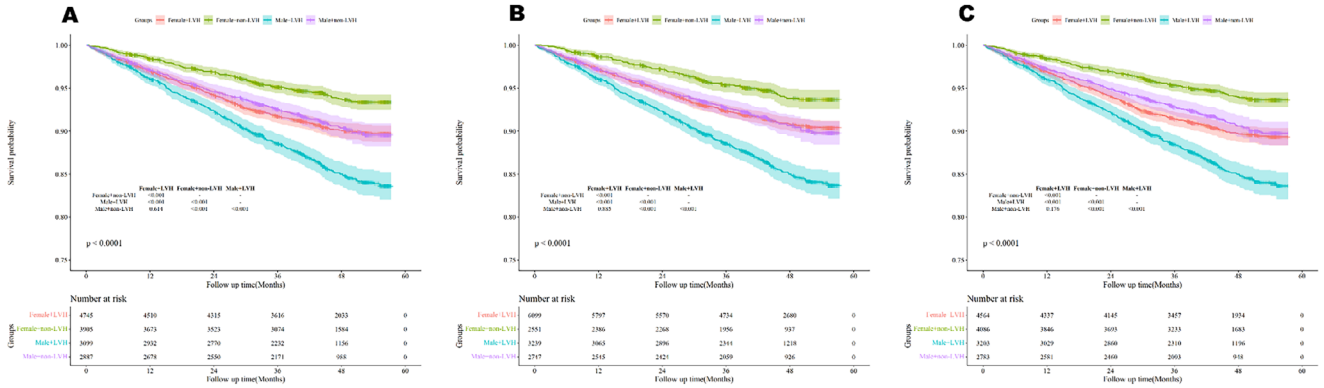

FIGURE 2 | Sex-specific Kaplan–Meier survival curves for patients with or without LVH for MACE. (A) for LVH indexed to BSA. (B) for LVH indexed to $H^{1.7}$. (C) for the LVH indexed to $H^{2.7}$. $p < 0.05$ is considered statistically significant. BSA, body surface area; H, height; LVH, left ventricular hypertrophy; MACE, major adverse cardiovascular events.

with LVH, women exhibited a reduced risk of MACE as demonstrated in Table S2, which was not observed in those without LVH.

3.4 | CV Prognosis and LVH Geometric Patterns in Women and Men

In the fully adjusted model, when LVM indexed to BSA, both concentric hypertrophy (adjusted hazard ratio [aHR]: 1.73, 95% CI: 1.37–2.19; $p < 0.001$) and eccentric hypertrophy (aHR: 1.54, 95% CI: 1.06–2.25; $p = 0.025$) were significantly associated with MACE in men. In women, eccentric hypertrophy showed borderline statistical significance (aHR: 1.26, 95% CI: 1.00–1.58; $p = 0.05$) for MACE (Table 4). Further analysis indicated that women with concentric hypertrophy had a significantly lower risk of MACE than men (aHR:0.66, 95% CI:0.48–0.91; $p < 0.001$) when LVM was indexed to BSA. In addition, women with eccentric hypertrophy had a lower risk of MACE (aHR: 0.53, 95% CI: 0.38–0.73; $p = 0.01$) compared with men when LVM was indexed to height$^{1.7}$(Table S3).

3.5 | Sensitivity Analysis

After applying the Chinese thresholds, the results remained consistent (Tables S6–S9). Regardless of the LVH definition used, both men and women with LVH exhibited a significantly higher risk of MACE after multivariable adjustment for covariate, with men consistently demonstrating a higher risk than women. Specifically, when LVH was defined using LVM indexed to BSA, the risk of MACE in men was 32% higher compared with women (HR = 1.56, 95% CI: 1.31–1.85 vs. HR = 1.24, 95% CI: 1.04–1.49). Among LVH patients, concentric hypertrophy was associated with the greatest risk of MACE. Women remained a protective factor among participants with LVH.

Notably, the number of individuals diagnosed with LVH was lower when using the Chinese thresholds compared with the guideline thresholds (Table S5).

4 | Discussion

In this prospective cohort study, we found that the prevalence of LVH was higher in women than in men. Among the various geometric patterns of LVH, women exhibited a greater prevalence of both eccentric and concentric hypertrophy, while men showed a higher prevalence of left ventricular remodeling when LVM was indexed to BSA. Our study demonstrated that higher BP and previous DM were associated with an increased risk of LVH in both genders, while aging and adiposity had a more hazardous impact on women compared to men. Furthermore, LVH was significantly associated with a higher risk of MACE in men than in women.

Our findings indicate that the impact of disease on the myocardium differs between men and women, suggesting that geometric remodeling of the myocardium varies by sex. Among high-risk CVD patients, women were more likely to develop eccentric and concentric hypertrophy, while men tended to exhibit concentric remodeling when indexed to BSA. This finding aligns with previous studies of patients with type 2 diabetes mellitus (T2DM) [19]. Kuneman et al. also reported that in patients with severe aortic stenosis, men exhibited a higher prevalence of concentric remodeling, although no differences between sexes were observed in the other LV geometric patterns [20]. However, the common finding in CMR imaging studies is that women had a higher prevalence of concentric remodeling [4, 21]. One possible explanation is that the differences in normalization methods and threshold definitions may account for this variation [22]. Additionally, the population in our study was younger and had fewer comorbidities than those in other studies. Generally, these findings offered solid evidence of sex-specific influences on the pathways of cardiac remodeling. Further research is needed to clarify the underlying pathophysiological mechanisms.

Our study showed that risk factors, including high BP, previous DM, high TG level, and aging were associated with a higher prevalence of LVH in both sexes while being overweight and obese evaluated by BMI had a more pronounced impact on the risk of LVH in women than in men. Elevated BP and previous DM are closely related to and well-documented associations for the development of LVH and cardiac geometric changes [5, 23, 24]. Additionally, higher TG levels increased the risk of LVH by 25%–27% [6, 25], while advancing age is associated with a 1.5-fold greater risk in women than in men [26]. Furthermore, the presence of obesity carried higher risk for LVH in women

TABLE 3 | Sex-specific Cox regression on LVH in predicting MACE.

	Women			Men		
Regression analysis	**Case/Participants**	**HR (95% CI)**	***p* value**	**Case/Participants**	**HR (95% CI)**	***p* value**
LVM/BSA	654/8650			673/5986		
Unadjusted						
Non-LVH	216/3905	Ref.		248/2887	Ref.	
LVH	438/4745	1.66 (1.41–1.95)	<0.001	425/3099	1.59 (1.36–1.85)	<0.001
Adjusted						
Non-LVH	216/3905	Ref.		248/2887	Ref.	
LVH	438/4745	1.11 (0.94–1.32)	0.203	425/3099	1.25 (1.06–1.46)	0.007
LVH/$H^{1.7}$	654/8650			673/5986		
Unadjusted						
Non-LVH	131/2551	Ref.		229/2747	Ref.	
LVH	523/6099	1.63 (1.34–1.97)	<0.001	444/3239	1.63 (1.39–1.91)	<0.001
Adjusted						
Non-LVH	131/2551	Ref.		229/2747		
LVH	523/6099	1.01 (0.83–1.24)	0.906	444/3239	1.28 (1.09–1.51)	0.003
LVH/$H^{2.7}$	654/8650			673/5986		
Unadjusted						
Non-LVH	218/4086	Ref.		231/2783	Ref.	
LVH	436/4564	1.79 (1.52–2.11)	<0.001	442/3203	1.65 (1.41–1.94)	<0.001
Adjusted						
Non-LVH	218/4086	Ref.		231/2783	Ref.	
LVH	436/4564	1.16 (0.98–1.38)	0.087	442/3203	1.30 (1.10–1.53)	0.002

Notes: Multivariable Logistics regression analysis was adjusted for age, SBP, DBP, HR, BMI, current smoker, current drinker, education status, occupation, residence, family annual income, marriage, insurance, physical exercise, FBG, TG, LDL-C, TC, HDL-C, treatment (antihypertensive treatment, hypoglycemic treatment, dyslipidemia treatment), HTN, DM, and dyslipidemia. BMI was not included while using LVM/BSA; however, BMI was included as covariate when indexing LVM to $H^{1.7}$ or $H^{2.7}$.

Abbreviations: BMI, body mass index; BSA, body surface area; CI, confidence intervals.; DBP, diastolic blood pressure; DM, diabetes mellitus; FBG, fasting blood glucose; $H^{1.7}$, $height^{1.7}$; $H^{2.7}$, $height^{2.7}$; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; HR, heart rate; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; LVM, left ventricular mass; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

compared with men, which was in line with previous data from echocardiography and CMR imaging studies [11, 27, 28]. Various issues may account for this observation. Firstly, the hemodynamics of obesity involve increased blood volume and elevated BP, leading to pressure overload. Thus, the LV response to the pressure overload leading to LVH [29, 30]. Secondly, sex hormones are also essential factors on BMI differences responsible for sex-specific cardiovascular changes including interstitial fibrosis and increased LV stiffness [5, 31]. This phenomenon may also elucidate the increase in LV mass that occurs with aging in women, particularly during the menopausal period.

In the present study, LVH was associated with MACE only in men when using guideline thresholds, whereas it was associated with MACE in both sexes using Chinese thresholds, with a higher risk observed in men. Interestingly, in the population with LVH, it was shown that women exhibited a decreased risk for MACE. Recent research in hypertensive patients found that after a 4-year follow-up, women without LVH had a 35% lower risk of MACE compared to men, whereas no sex differences were observed in cardiovascular event risk among individuals with LVH [11]. The LIFE study demonstrated cardiovascular events were 35% lower in women than in men [32].

Notably, Zhou et al. reported that the Chinese thresholds outperformed guideline thresholds in predicting cardiovascular events among individuals with LVH, whereas the use of guideline thresholds may substantially overestimate the prevalence of LVH [22]. Consistently, our study also found a significant decrease in the number of people identified as having LVH when using the Chinese thresholds. Additionally, these criteria improved the identification of individuals at risk for MACE. Zhang et al. [18] have also emphasized the necessity of using ethnicity-specific LVH thresholds. These results highlight the need for future research implementing diagnostic criteria that are both sex-specific and adapted to the local population to enhance diagnostic precision and prognostic value.

Furthermore, concentric and eccentric hypertrophy were significantly associated with MACE in men when indexed to BSA.

TABLE 4 | Sex-specific Cox regression on LVH geometric patterns in predicting MACE.

Regression analysis	Women			Men		
	Case/ Participants	HR (95% CI)	*p* value	Case/ Participants	HR (95% CI)	*p* value
LVM/BSA	654/8650			673/5986		
Unadjusted						
Normal geometry	216/3689	Ref.		248/2887	Ref.	
Concentric hypertrophy	158/1400	2.016 (1.642–2.475)	<0.001	109/481	2.759 (2.202–3.456)	<0.001
Eccentric hypertrophy	114/1134	1.780 (1.418–2.233)	<0.001	31/165	2.196 (1.512–3.190)	<0.001
Concentric remodeling	166/2211	1.368 (1.118–1.675)	0.002	285/2453	1.328 (1.121–1.575)	0.001
Adjusted						
Normal geometry	216/3689	Ref.		248/2887	Ref.	
Concentric hypertrophy	158/1400	1.130 (0.913–1.397)	0.261	109/481	1.730 (1.369–2.187)	<0.001
Eccentric hypertrophy	114/1134	1.258 (1.000–1.584)	0.050	31/165	1.540 (1.055–2.246)	0.025
Concentric remodeling	166/2211	1.026 (0.836–1.258)	0.808	285/2453	1.116 (0.939–1.325)	0.214
LVM/$H^{1.7}$	654/8650			673/5986		
Unadjusted						
Normal geometry	243/3172	Ref.		230/2126	Ref.	
Concentric hypertrophy	140/1745	1.049 (0.852–1.291)	0.656	148/1275	1.071 (0.871–1.316)	0.518
Eccentric hypertrophy	120/1633	0.914 (0.734–1.137)	0.420	134/1160	1.028 (0.831–1.272)	0.800
Concentric remodeling	151/2100	0.953 (0.778–1.168)	0.644	161/1425	1.074 (0.878–1.313)	0.490
Adjusted						
Normal geometry	243/3172	Ref.		230/2126	Ref.	
Concentric hypertrophy	140/1745	1.008 (0.818–1.242)	0.943	148/1275	1.061 (0.863–1.306)	0.573
Eccentric hypertrophy	120/1633	0.911 (0.731–1.134)	0.403	134/1160	1.046 (0.845–1.296)	0.678
Concentric remodeling	151/2100	0.914 (0.745–1.121)	0.387	161/1425	1.059 (0.865–1.297)	0.577
LVM/$H^{2.7}$	654/8650			673/5986		
Unadjusted						
Normal geometry	310/4122	Ref.		307/2747	Ref.	
Concentric hypertrophy	85/1131	1.014 (0.797–1.290)	0.911	93/797	1.082 (0.858–1.365)	0.504
Eccentric hypertrophy	53/683	1.017 (0.760–1.360)	0.912	57/539	0.929 (0.700–1.233)	0.611
Concentric remodeling	207/2714	1.037 (0.870–1.237)	0.685	216/1903	1.035 (0.970–1.232)	0.698
Adjusted						
Normal geometry	310/4122	Ref.		307/2747	Ref.	
Concentric hypertrophy	85/1131	0.966 (0.758–1.231)	0.779	93/797	1.065 (0.944–1.344)	0.595
Eccentric hypertrophy	53/683	1.050 (0.784–1.406)	0.743	57/539	0.946 (0.713–1.257)	0.703
Concentric remodeling	207/2714	1.007 (0.843–1.201)	0.943	216/1903	1.021 (0.857–1.216)	0.818

Notes: Multivariable Logistics regression analysis was adjusted for age, SBP, DBP, HR, BMI, current smoker, current drinker, education status, occupation, residence, family annual income, marriage, insurance, physical exercise, FBG, TG, LDL-C, TC, HDL-C, treatment (antihypertensive treatment, hypoglycemic treatment, dyslipidemia treatment), HTN, DM, and dyslipidemia. BMI was not included while using LVM/BSA; however, BMI was included as covariate when indexing LVM to $H^{1.7}$ or $H^{2.7}$.

Abbreviations: BMI, body mass index; BSA, body surface area; CI, confidence intervals.; DBP, diastolic blood pressure; DM, diabetes mellitus; FBG, fasting blood glucose; $H^{1.7}$, $height^{1.7}$; $H^{2.7}$, $height^{2.7}$; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; HR, heart rate; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; LVM, left ventricular mass; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

In individuals with concentric hypertrophy (LVM/BSA) and eccentric hypertrophy (LVM/H1.7), women exhibited a lower risk of MACE than men. Framingham Heart study found that individuals, particularly in men, with concentric hypertrophy were related to an elevated risk of all-cause mortality and incident CVD in participants (≥40 years old) free of clinically apparent CVD [33]. At a median follow-up of 3.7 years in patients with known or suspected CAD, concentric hypertrophy was associated with higher all-cause mortality in both sexes, but eccentric hypertrophy was associated with all-cause mortality exclusively in women [4]. Capoulade et al. demonstrated that concentric hypertrophy was associated with higher risk of all-cause mortality in women, but was neutral in men with aortic stenosis [34]. The study mentioned above indicated that there was lack of consensus on the sex-specific prognosis of LVH geometric patterns. The association can differ based on factors such as the characteristics of the study population, duration of follow-up, and diagnostic techniques for LVH. Though the development of cardiac hypertrophy differ between sexes was well-established. Many of these sex deviations are driven by the presence or absence of sex hormones. Still, other variables, such as sex chromosomes and epigenetics, can also influence unfavorable cardiac remodeling in a sex-specific manner [35]. Besides, gender discrepancies may arise from differences in the applicability of European LV remodeling definitions to Asian populations [22]. Therefore, additional research is necessary to clarify the processes that explain these sex-specific associations.

Our study has several notable strengths. First, we employed a substantial, community-based, high-risk CVD population enrolled from the China PEACE-MPP in Guangdong province, which enhanced result reliability and expanding research in Asian populations. Moreover, we examine various definitions of LVH rather than relying on one definition method, as well as sex-specific LVH geometric patterns and their prognostic implications. There are several limitations inherent to our investigation. Firstly, it should be noted that the follow-up period in the available studies is relatively short. Therefore, further research is necessary to determine the long-term effects of LVH in relation to sex specificity. Additionally, the comprehensive collection of physical and laboratory examination data was limited to the baseline assessment, which hinders the evaluation of any changes in these data throughout the follow-up period. Furthermore, the potential differential effects of specific antihypertensive drug classes on cardiovascular outcomes were not included in our study due to lack of this data. Lastly, since all participants in this study are Han Chinese from Guangdong province, we need to be careful about applying our findings to other ethnic groups.

5 | Conclusion

Our findings underscore the importance of managing risk factors, including BP, blood glucose, lipids level, and BMI with advanced age. Sex differences also lead to different geometric patterns of LVH which predict cardiovascular outcomes. Men should pay more attention to the occurrence of LVH, which has a greater association with MACE. These insights support the need for sex-specific LVH prevention strategies to better address the global burden of CVD.

Author Contributions

All authors have made an important scientific contribution to the study and have no conflicts of interest to disclose. Yingqing Feng, Xiaoxuan Feng, Shiping Wu, Jiabin Wang participated in study design. Xiaoxuan Feng, Shiping Wu, Jiabin Wang, Mengqi Yan, Dan Zhou, and Yingqing Feng contributed to data analysis and interpretation. Shiping Wu, Xiaoxuan Feng, He Zheng, Dan Zhou, and Yingqing Feng were responsible for drafting the manuscript or revising it critically for important intellectual content. All authors listed have read and approved submission of the paper.

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Ethics Statement

This study was approved by both the Central Ethics Committee at the China National Center for Cardiovascular Disease and the Ethics Committee of Guangdong Provincial People's Hospital [No. GDREC2016438H (R2)].

Consent

Written informed consents were obtained from all participants.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data Availability Statement

The data underlying this article cannot be shared publicly considering the privacy of individuals that participated in the study. The data and underlying code can be shared on reasonable request to the corresponding author.

References

1. M. H. Stewart, C. J. Lavie, S. Shah, et al., "Prognostic Implications of Left Ventricular Hypertrophy," *Progress in Cardiovascular Diseases* 61, no. 5-6 (2018): 446–455.

2. R. M. Lang, L. P. Badano, V. Mor-Avi, et al., "Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update From the American Society of Echocardiography and the European Association of Cardiovascular Imaging," *Journal of the American Society of Echocardiography* 28, no. 1 (2015): 1–39.e14.

3. R. L. Antikainen, R. Peters, N. S. Beckett, et al., "Left Ventricular Hypertrophy Is a Predictor of Cardiovascular Events in Elderly Hypertensive Patients: Hypertension in the Very Elderly Trial," *Journal of Hypertension* 34, no. 11 (2016): 2280–2286.

4. R. J. H. Miller, Y. Mikami, B. Heydari, et al., "Sex-Specific Relationships Between Patterns of Ventricular Remodelling and Clinical Outcomes," *European Heart Journal Cardiovascular Imaging* 21, no. 9 (2020): 983–990.

5. M. Tadic, C. Cuspidi, and G. Grassi, "The Influence of Sex on Left Ventricular Remodeling in Arterial Hypertension," *Heart Failure Reviews* 24, no. 6 (2019): 905–914.

6. X. W. Huang, K. Q. Deng, J. J. Qin, et al., "Association Between Lipid Profiles and Left Ventricular Hypertrophy: New Evidence From a Retrospective Study," *Chinese Medical Sciences Journal = Chung-kuo i Hsueh K'o Hsueh Tsa Chih* 37, no. 2 (2022): 103–117.

7. J. Lv, Y. Liu, Y. Yan, et al., "Relationship Between Left Ventricular Hypertrophy and Diabetes Is Likely Bidirectional: A Temporality Analysis," *Journal of the American Heart Association* 12, no. 6 (2023): e028219.

8. D. E. Manyari, "Prognostic Implications of Echocardiographically Determined Left Ventricular Mass in the Framingham Heart Study," *New England Journal of Medicine* 323, no. 24 (1990): 1706–1707.

9. R. V. Milani, C. J. Lavie, M. R. Mehra, H. O. Ventura, J. D. Kurtz, and F. H. Messerli, "Left Ventricular Geometry and Survival in Patients With Normal Left Ventricular Ejection Fraction," *American Journal of Cardiology* 97, no. 7 (2006): 959–963.

10. J. K. Ghali, Y. Liao, and R. S. Cooper, "Influence of Left Ventricular Geometric Patterns on Prognosis in Patients With or Without Coronary Artery Disease," *Journal of the American College of Cardiology* 31, no. 7 (1998): 1635–1640.

11. E. Gerdts, R. Izzo, C. Mancusi, et al., "Left Ventricular Hypertrophy Offsets the Sex Difference in Cardiovascular Risk (the Campania Salute Network)," *International Journal of Cardiology* 258 (2018): 257–261.

12. J. Lu, S. Xuan, N. S. Downing, et al., "Protocol for the China PEACE (Patient-Centered Evaluative Assessment of Cardiac Events) Million Persons Project Pilot," *BMJ Open* 6, no. 1 (2016): e010200.

13. J. Lu, Y. Lu, X. Wang, et al., "Prevalence, Awareness, Treatment, and Control of Hypertension in China: Data From 1·7 Million Adults in a Population-Based Screening Study (China PEACE Million Persons Project)," *Lancet (London, England)* 390, no. 10112 (2017): 2549–2558.

14. Organization WH, Organization WH. *International Society of Hypertension (WHO/ISH) Risk Prediction Charts for 14 WHO Epidemiological Sub-regions* (World Health Organization. 2007).

15. A. Cai, C. Chen, J. Wang, Y. Ou, Z. Nie, and Y. Feng, "Life's Essential 8 and Risk of Incident Heart Failure in Community Population Without Cardiovascular Disease: Results of the Sub-Cohort of China PEACE Million Persons Project," *Preventive Medicine* 178 (2024): 107797.

16. J. A. Chirinos, P. Segers, M. L. De Buyzere, et al., "Left Ventricular Mass: Allometric Scaling, Normative Values, Effect of Obesity, and Prognostic Performance," *Hypertension (Dallas, Tex: 1979)* 56, no. 1 (2010): 91–98.

17. A. Cai, J. Wang, X. Feng, et al., "Cardiovascular Disease Modifies the Relationship Between Systolic Blood Pressure and Outcomes in People With Diabetes," *Diabetes Research and Clinical Practice* 218 (2024): 111909.

18. Y. Sheng, M. Li, M. Xu, et al., "Left Ventricular and Atrial Remodelling in Hypertensive Patients Using Thresholds From International Guidelines and EMINCA Data," *European Heart Journal Cardiovascular Imaging* 23, no. 2 (2022): 166–174.

19. M. Z. Wu, Y. Chen, Y. J. Yu, et al., "Sex-specific Pattern of Left Ventricular Hypertrophy and Diastolic Function in Patients With Type 2 Diabetes Mellitus," *European Heart Journal Cardiovascular Imaging* 22, no. 8 (2021): 930–940.

20. J. H. Kuneman, G. K. Singh, S. Milhorini Pio, et al., "Sex Differences in Left Ventricular Remodelling in Patients With Severe Aortic Valve Stenosis," *European Heart Journal Cardiovascular Imaging* 23, no. 6 (2022): 781–789.

21. T. A. Treibel, R. Kozor, M. Fontana, et al., "Sex Dimorphism in the Myocardial Response to Aortic Stenosis," *JACC: Cardiovascular Imaging* 11, no. 7 (2018): 962–973.

22. D. Zhou, M. Yan, A. Cai, et al., "Prognostic Implications of Left Ventricular Hypertrophy Defined by the Thresholds From the International and Chinese Guidelines," *Journal of Clinical Hypertension (Greenwich, Conn.)* 25, no. 7 (2023): 628–637.

23. S. Kishi, S. S. Gidding, J. P. Reis, et al., "Association of Insulin Resistance and Glycemic Metabolic Abnormalities With LV Structure and Function in Middle Age: The CARDIA Study," *JACC Cardiovascular Imaging* 10, no. 2 (2017): 105–114.

24. V. H. Schmitt, A. M. Billaudelle, A. Schulz, et al., "Disturbed Glucose Metabolism and Left Ventricular Geometry in the General Population," *Journal of Clinical Medicine* 10, no. 17 (2021): 3851.

25. J. Sundström, L. Lind, B. Vessby, B. Andrén, A. Aro, and H. Lithell, "Dyslipidemia and an Unfavorable Fatty Acid Profile Predict Left Ventricular Hypertrophy 20 Years Later," *Circulation* 103, no. 6 (2001): 836–841.

26. M. Yan, S. Sun, K. Xu, et al., "Cardiac Aging: From Basic Research to Therapeutics," *Oxidative Medicine and Cellular Longevity* 2021 (2021): 9570325.

27. C. Cuspidi, M. Rescaldani, C. Sala, and G. Grassi, "Left-ventricular Hypertrophy and Obesity: A Systematic Review and Meta-analysis of Echocardiographic Studies," *Journal of Hypertension* 32, no. 1 (2014): 16–25.

28. G. De Simone, R. B. Devereux, M. Chinali, et al., "Sex Differences in Obesity-Related Changes in Left Ventricular Morphology: The Strong Heart Study," *Journal of Hypertension* 29, no. 7 (2011): 1431–1438.

29. W. B. Drøyvold, K. Midthjell, T. I. Nilsen, and J. Holmen, "Change in Body Mass Index and Its Impact on Blood Pressure: A Prospective Population Study," *International Journal of Obesity (2005)* 29, no. 6 (2005): 650–655.

30. T. Wilsgaard, H. Schirmer, and E. Arnesen, "Impact of Body Weight on Blood Pressure With a Focus on Sex Differences: The Tromso Study, 1986–1995," *Archives of Internal Medicine* 160, no. 18 (2000): 2847–2853.

31. R. Cifkova, J. Pitha, A. Krajcoviechova, and E. Kralikova, "Is the Impact of Conventional Risk Factors the Same in Men and Women? Plea for a More Gender-Specific Approach," *International Journal of Cardiology* 286 (2019): 214–219.

32. I. Os, V. Franco, S. E. Kjeldsen, et al., "Effects of Losartan in Women With Hypertension and Left Ventricular Hypertrophy: Results From the Losartan Intervention for Endpoint Reduction in Hypertension Study," *Hypertension (Dallas, Tex: 1979)* 51, no. 4 (2008): 1103–1108.

33. H. M. Krumholz, M. Larson, and D. Levy, "Prognosis of Left Ventricular Geometric Patterns in the Framingham Heart Study," *Journal of the American College of Cardiology* 25, no. 4 (1995): 879–884.

34. R. Capoulade, M. A. Clavel, F. Le Ven, et al., "Impact of Left Ventricular Remodelling Patterns on Outcomes in Patients With Aortic Stenosis," *European Heart Journal Cardiovascular Imaging* 18, no. 12 (2017): 1378–1387.

35. E. L. Kessler, M. R. Rivaud, M. A. Vos, and T. A. B. van Veen, "Sex-Specific Influence on Cardiac Structural Remodeling and Therapy in Cardiovascular Disease," *Biology of Sex Differences* 10, no. 1 (2019): 7.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.