Check for updates

Effect of Obesity on Left Ventricular Remodeling and Clinical Outcome in Chinese Patients With Hypertrophic Cardiomyopathy: Assessed by Cardiac MRI

Ke Shi, MD,[1] Shan Huang, MD,[1] Xiang Li, MS,[1] Hua-Yan Xu, MD,[2] Meng-Xi Yang, MD,[1,3] Yuan Li, MD,[1] Ying-Kun Guo, MD, PhD,[2] and Zhi-Gang Yang, MD, PhD[1]*

Background: Obesity is highly prevalent in patients with hypertrophic cardiomyopathy (HCM) and believed to influence its phenotype.
Purpose: To explore the effects of obesity on left ventricular (LV) remodeling and long-term clinical course in Chinese patients with HCM.
Study Type: Longitudinal.
Population: A total of 247 patients with HCM classified according to body mass index (BMI) (normal weight: BMI = 18.0–22.9 kg/m^2 [N = 90]; overweight: BMI = 23.0–24.9 kg/m^2 [N = 58]; and obese: BMI ≥ 25 kg/m^2 [N = 99]).
Field Strength/Sequence: 3.0 T/Balanced steady-state free precession sequence and phase-sensitive inversion recovery late gadolinium enhancement (LGE) sequence.
Assessment: LV function and geometry were measured. LV peak strain analysis was performed. The presence and percentage of LGE in the LV were recorded. The endpoints including heart failure, sudden cardiac death, and overall composite outcome were assessed during a median follow-up of 4.1 years (interquartile range, 3.0–6.2 years).
Statistical Tests: One-way analysis of variance, Kruskal–Wallis test, or chi-square test; Pearson correlation coefficient (r); multivariable linear regression analysis; Kaplan–Meier survival analysis; and Cox proportional hazards model analysis were conducted. A two-tailed P-value < 0.05 was considered statistically significant.
Results: Obese patients exhibited a significant progressive increase in LV mass compared with normal-weight patients. The magnitude of all LV strain indices gradually and significantly decreased as BMI increased, whereas LV ejection fraction was not significantly different among BMI groups (P = 0.364). Multivariable linear regression analysis showed that obesity had a significant association with impaired strain indices as well as with indexed LV mass. Multivariable Cox model analysis retained obesity as an independent marker for future endpoints, and conveyed a > 3-fold increase in risk compared with patients with normal weight (hazard ratio, 3.04; 95% confidence interval, 1.07–6.57).
Data Conclusion: Obesity is an important environmental modifier that is associated with adverse LV remodeling and is independently associated with future clinical outcomes in Chinese patients with HCM.
Level of Evidence: 3
Technical Efficacy: Stage 2

J. MAGN. RESON. IMAGING 2023;57:800–809.

Hypertrophic cardiomyopathy (HCM) is a primary myocardial disorder characterized by left ventricular (LV) hypertrophy that develops without known predisposing cause.[1] In most individuals with inherited HCM, it is caused by mutations in one of the genes encoding cardiac sarcomere proteins.[1] However, gene mutation is not the sole determinant of

View this article online at wileyonlinelibrary.com. DOI: 10.1002/jmri.28306

Received Apr 20, 2022, Accepted for publication Jun 2, 2022.

*Address reprint requests to: Z.-G.Y., Department of Radiology, West China Hospital, Sichuan University, Chengdu, Sichuan, China. E-mail: yangzg666@163.com

From the [1]Department of Radiology, Functional and Molecular Imaging Key Laboratory of Sichuan Province, West China Hospital, Sichuan University, Chengdu, Sichuan, China; [2]Department of Radiology, Key Laboratory of Birth Defects and Related Diseases of Women and Children of Ministry of Education, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China; and [3]Department of Radiology, Sichuan Cancer Hospital and Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, Chengdu, Sichuan, China

Additional supporting information may be found in the online version of this article

 © 2022 International Society for Magnetic Resonance in Medicine.

disease expression, as epigenetic and environmental factors are also thought to be responsible for the heterogeneous phenotypes and diverse clinical outcomes of HCM.[2–4]

Obesity has become a worldwide pandemic, and is an established risk factor for almost all cardiovascular diseases because of its adverse effects on cardiac structure and function.[3] In patients with HCM, obesity prevalence is almost 40%.[2] One reason for such a high prevalence is that most of these patients are concerned that exercise may trigger fatal arrhythmias or sudden cardiac death (SCD) and thus choose to reduce or even stop physical activity after diagnosis.[2,5,6] While some studies have reported that obesity may contribute to the development of heart failure (HF) and occurrence of adverse clinical outcomes, a better understanding of the effect of obesity on HCM phenotype modulation is of importance.[7,8] However, there is limited data on changes in contractile function and LV remodeling in obese patients.

Thus, the aim of this study was to examine the potential effect of obesity on myocardial mechanics, LV remodeling, and long-term clinical outcomes in patients with HCM who underwent cardiac magnetic resonance imaging (MRI).

Materials and Methods

Study Population

This study was approved by the Biomedical Research Ethics Committees of our hospital. Written informed consent was waived off because of the retrospective nature of the study. All medical data were protected with full confidentiality and used only for the purpose of the present study.

A retrospective cohort of 316 patients who were admitted to our hospital between June 2012 and December 2019 were eligible for study inclusion. HCM was diagnosed based on the following established criteria: 1) LV wall thickness (WT) of ≥ 15 mm or ≥ 13 mm in patients with a family history of HCM and 2) no known predisposing cause of LV hypertrophy (LVH), such as aortic stenosis, or amyloidosis.[9] In addition, patients with hypertension were considered to have HCM if they met at least one of the following conditions[7,10]: onset of hypertension after the diagnosis of HCM; detection of a family history of HCM; maximum LVWT exceeding that caused by hypertension alone (LVWT ≥ 20 mm); dynamic LV outflow tract gradient (LVOT) ≥ 30 mmHg at rest; and distribution of late gadolinium enhancement (LGE) consistent with HCM (localized at the right ventricular insertion points or to segments of maximum LV thickening). We excluded patients who had undergone prior septal myectomy or alcohol septal ablation and those with incomplete medical records, or unevaluable MRI. Finally, 247 patients with HCM were included for analysis.

Patients were then classified according to body mass index (BMI) as normal weight, overweight, or obese. Since Asian individuals generally have a higher percentage of body fat than Caucasian individuals of the same age, sex, and BMI, we applied the BMI cut-off values proposed by the World Health Organization for Asian populations: normal weight, BMI = 18.0–22.9 kg/m^2; overweight, BMI = 23.0–24.9 kg/m^2; and obese, BMI ≥ 25 kg/m^2.[3] The study design is shown in Fig. 1.

The clinical characteristics, laboratory data (including plasma concentration of triglycerides, cholesterol, and NT-proBNP), and medications of all 247 patients were obtained by searching the electronic clinical database of our hospital.

MRI Protocol

MRI was performed on a 3-T scanner (MAGNETOM Skyra/Tim Trio; Siemens Healthcare, Erlangen, Germany) with data being obtained during breath-hold periods. Cine imaging was performed in the two-chamber long-axis slices, four-chamber long-axis slices, and in 8–12 contiguous two-chamber short-axis slices from the mitral valve to the LV apex using a retrospectively segmented ECG-gated balance steady state free precession sequence with the following parameters: repetition time (TR) = 2.81 msec; echo time (TE) = 1.22 msec; slice thickness = 8.0 mm; flip angle (FA) = 40°/50°; acquisition matrix = 166 × 208 pixels; and field of

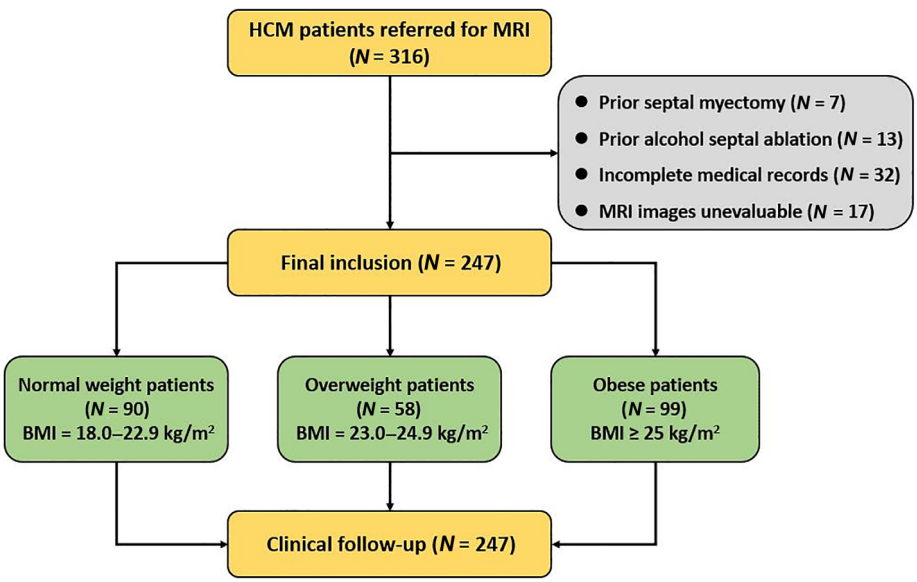

FIGURE 1: Study design of the entire project. HCM, hypertrophic cardiomyopathy; BMI, body mass index.

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

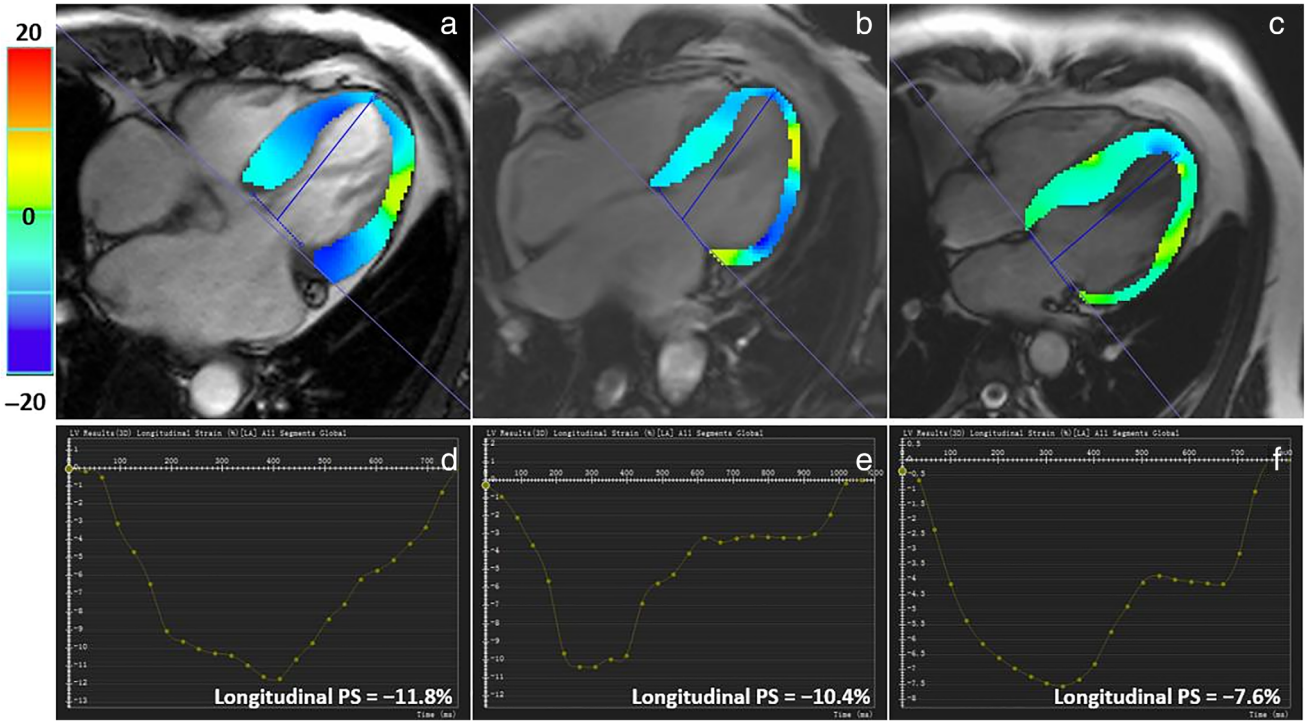

FIGURE 2: Examples cardiac MRI images of normal weight (a, d), overweight (b, e), and obese (c, f) patients with HCM. a–c, four-chamber long-axis cine images of LV when performing strain analysis; d–f, corresponding derived global longitudinal PS curves. HCM, hypertrophic cardiomyopathy; LV, left ventricular; PS, peak strain.

view (FOV) = 340 × 284 mm^2. Twenty-five frames were reconstructed per breath-hold acquisition for cine images. LGE imaging was performed 15 minutes after the administration of gadolinium-based contrast (gadobenate dimeglumine [MultiHance; Bracco, Milan, Italy], 0.2 mmol/kg) using a phase-sensitive inversion recovery sequence with the following parameters: TR = 700 msec; TE = 1.18 msec; slice thickness = 8.0 mm; FA = 40°/20°; acquisition matrix = 184 × 256 pixels; and FOV = 350 × 295 mm^2. LGE images were acquired with breath-holding maneuver.

Imaging Analysis

Data was analyzed using CVI[42] software (Circle Cardiovascular Imaging, Inc., Calgary, Alberta, Canada) by two investigators (K.S. with 9 years and S.H. with 6 years of cardiac MRI experience) who were blind to the results from each other. The interobserver reproducibility of measurement for the MRI indices was good, with intraclass correlation coefficients ranged from 0.90 to 0.95. In a series of short-axis images, endocardial and epicardial borders were manually drawn at the LV end-diastolic and end-systolic phases, respectively. LV function parameters, including ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV), and stroke volume (SV) were automatically calculated. LV mass (LVM) was assessed by measuring the area between the endocardial and epicardial borders in each of the short-axis slices. LV papillary muscles were included in the LVM but not in the LV volume. LV function parameters and LVM were indexed to body surface area. Maximum LVWT measurements were performed at the end-diastolic phase. Two-chamber and four-chamber long-axis cine images, combined with short-axis cine images, were loaded into the feature-tracking module for LV strain analysis. By delineating LV endocardial and epicardial borders at the end-diastolic phases (reference phase) of all cine images, long-axis cine images were used to derive global longitudinal peak strain (PS), whereas short-axis cine images were used to derive global radial and circumferential PS.[11] The short-axis reference points were inserted at the upper and lower septal insertion of the LV for global analysis of strain. Then, the software automatically traced and drew the contours throughout the remaining cardiac cycle. The representatives of normal weight, overweight, and obese subgroups with HCM were shown in Fig. 2. LGE images were semi-automatically quantified using the established grayscale threshold method of six standard deviations exceeding the mean signal intensity of remote nonfibrotic myocardium.[12]

Follow-Up and Endpoints

We used three composite endpoints to maximize statistical power: 1) HF composite outcome: advanced HF; 2) SCD composite outcome: SCD, resuscitated cardiac arrest, and appropriate implantable cardioverter-defibrillator (ICD) therapy; and 3) overall composite outcome: HF-related death, all-cause mortality, and stroke. Advanced HF was defined as progression to New York Heart Association (NYHA) class III/IV symptoms. SCD was defined as unexpected death occurring within 1 hour of cardiac symptom onset in patients with a previously stable clinical course. Ventricular fibrillation or tachycardia that caused ICD intervention was considered equivalent to SCD. HF-related death was defined as death occurring in the setting of progressive cardiac decompensation. Follow-up data was obtained from the electronic medical records or phone calls to patients or family members. Follow-up duration was defined as the time from study entry to the occurrence of any endpoint or January 2021 (end of the study period).

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of the Study Population According to BMI Class

	Normal Weight (N = 90)	Overweight (N = 58)	Obesity (N = 99)	*P*-Value
Age, years	51.8 ± 16.1	54.3 ± 12.9	54.4 ± 13.2	0.399
Male, *N* (%)	33 (36.7)	36 (62.1)[§]	60 (60.6)[§]	0.001
BMI, kg/m^2	20.8 ± 1.7	24.1 ± 0.5*[,†]	27.6 ± 2.1*[,†]	< 0.001
Heart rate, bpm	68.4 ± 10.2	70.9 ± 11.0	70.4 ± 11.9	0.329
SBP, mmHg	118.0 ± 21.2	126.2 ± 19.8*	124.7 ± 17.6*	0.020
DBP, mmHg	70.6 ± 12.2	78.2 ± 11.8*	75.3 ± 11.9*	0.001
NYHA functional class, *N* (%)				
I	39 (43.3)	23 (39.7)	24 (24.2)	0.010
II	51 (56.7)	33 (56.9)	70 (70.7)[§,λ]	
III	0	2 (3.4)	5 (5.1)	
Unexplained scope, *N* (%)	31 (34.4)	19 (32.8)	22 (22.2)	0.153
NSVT, *N* (%)	13 (14.4)	7 (12.1)	17 (17.2)	0.677
History of AF, *N* (%)	7 (7.8)	5 (8.6)	13 (13.1)	0.471
Family history of HCM, *N* (%)	6 (6.7)	5 (8.6)	8 (8.1)	0.894
Family history of SCD, *N* (%)	2 (2.2)	1 (1.7)	2 (2.0)	1.00
LVOTO, *N* (%)	42 (46.7)	28 (48.3)	58 (58.6)	0.224
Smoking, *N* (%)	18 (20.0)	21 (36.2)[§]	40 (40.4)[§]	0.008
Drinking, *N* (%)	10 (11.1)	18 (31.0)[§]	24 (24.2)[§]	0.009
Co-morbidities, *N* (%)				
Hypertension	23 (25.6)	30 (51.7)[§]	44 (44.4)[§]	0.003
Diabetes mellitus	6 (6.7)	5 (8.6)	12 (12.1)	0.427
Medications, *N* (%)				
Beta-blocker	72 (80.0)	53 (91.4)	85 (85.9)	0.157
CCB	10 (11.1)	7 (12.1)	15 (15.2)	0.696
ACEI/ARB	17 (18.9)	12 (20.7)	24 (24.2)	0.666
Diuretics	24 (26.7)	9 (15.5)	22 (22.2)	0.297
Statins	16 (17.8)	19 (32.8)[§]	48 (48.5)[§]	< 0.001
Laboratory data				
TG, mmol/L	1.1 (0.8, 1.6)	1.4 (1.0, 2.2)[&]	1.6 (1.1, 2.1)[&]	< 0.001
TC, mmol/L	4.1 ± 0.9	4.3 ± 0.9	4.3 ± 1.0	0.335
NT-proBNP, pg/mL	879 (545, 1604)	909 (543, 1796)	1054 (513, 1961)	0.428

Data are presented as mean ± SD, median (IQR), or number (percentage).
One-way analysis of variance or Kruskal–Wallis test: **P*-value < 0.017 vs. normal weight cohort. [†]*P*-value < 0.017 vs. overweight cohort. [&]*P*-value < 0.05 vs. normal weight cohort.
Chi-square test (Fisher's exact test): [§]*P*-value < 0.05 vs. normal weight cohort. [λ]*P*-value < 0.05 vs. overweight cohort.
Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; NYHA, New York Heart Association; NSVT, nonsustained ventricular tachycardia; AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; SCD, sudden cardiac death; LVOTO, left ventricular outflow tract obstruction; CCB, calcium-channel blocker; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; TG, triglycerides; TC, cholesterol.

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. MRI Findings of the Study Population According to BMI Class

	Normal Weight (N = 90)	Overweight (N = 58)	Obesity (N = 99)	*P*-Value
LV EDV, mL	133.5 ± 27.8	157.9 ± 37.8*	155.7 ± 34.7*	< 0.001
LV EDVi, mL/m^2	90.0 ± 17.0	92.8 ± 19.6	88.1 ± 17.6	0.342
LV ESV, mL	48.9 ± 14.9	63.2 ± 22.7*	58.1 ± 19.3*	< 0.001
LV ESVi, mL/m^2	32.8 ± 9.4	36.3 ± 9.9	35.2 ± 10.9	0.139
LV SV, mL	84.6 ± 18.2	94.7 ± 22.9*	97.6 ± 22.6*	< 0.001
LV SVi, mL/m^2	57.1 ± 11.7	57.1 ± 13.4	55.3 ± 11.2	0.520
LV EF, %	63.6 ± 6.9	60.4 ± 7.8	62.9 ± 7.4	0.364
LVM, g	108.7 (93.1, 139.8)	131.4 (103.2, 159.4)$^{\&}$	153.5 (126.1, 188.9)$^{\&,£}$	< 0.001
LVMi, g/m^2	72.9 (61.8, 86.7)	79.4 (60.3, 100.3)	85.9 (72.6, 103.8)$^{\&}$	0.003
LVM/EDV ratio	0.8 (0.7, 1.0)	0.8 (0.7, 1.1)	1.0 (0.8, 1.2)$^{\&,£}$	< 0.001
Maximum LVWT, mm	18.0 ± 3.4	19.1 ± 4.5	19.1 ± 4.0	0.123
LA diameter, mm	44.9 ± 6.9	44.7 ± 8.1	46.3 ± 6.9	0.283
Phenotype of HCM, *N* (%)				
Asymmetric LVH	72 (80.0)	39 (67.2)§	62 (62.6)§	0.014
Symmetric LVH	15 (16.7)	16 (27.6)§	36 (36.4)§	
Apical LVH	3 (3.3)	3 (5.2)	1 (1.0)	
Presence of LGE, *N* (%)	38 (42.2)	26 (44.8)	45 (45.5)	0.907
LGE percentage of LVM, %	10.3 (6.3, 17.8)	12.5 (5.6, 16.4)	10.4 (6.2, 16.1)	0.989

Data are presented as mean ± SD, median (IQR), or number (percentage).
One-way analysis of variance or Kruskal–Wallis test: **P*-value < 0.017 vs. normal weight cohort. $^{\&}$*P*-value < 0.05 vs. normal weight cohort. $^{£}$*P*-value < 0.05 vs. overweight cohort.
Chi-square test (Fisher's exact test): §*P*-value < 0.05 vs. normal weight cohort.
Abbreviations: LV, left ventricular; EDV, end-diastolic volume; EDVi, indexed end-diastolic volume; ESV, end-systolic volume; EDVi, indexed end-systolic volume; SV, stroke volume; SVi, indexed stroke volume; EF, ejection fraction; LVM, left ventricular mass; LVMi, indexed left ventricular mass; WT, wall thickness; LA, left atrial; HCM, hypertrophic cardiomyopathy; LVH, left ventricular hypertrophy; LGE, late gadolinium enhancement.

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Statistical Analysis

The normality of data was determined using the Shapiro–Wilk test. Data are expressed as means with standard deviations or medians with interquartile ranges (IQRs) for continuous variables and frequencies for categorical variables. Clinical and MRI variables were compared among the BMI groups using one-way analysis of variance, followed by the Bonferroni post hoc test, Kruskal–Wallis test, or chi-square test (Fisher's exact test), as appropriate. Bivariable correlation coefficients (r) were obtained using the Pearson method. The determinants of impaired LV contractile function and ventricular remodeling were assessed using linear regression analysis. Candidate variables with $P < 0.10$ in the univariable analysis and the absence of collinearity were included in multivariable models. Long-term adverse outcomes were assessed using Kaplan–Meier survival analysis and compared among the groups using the log-rank test. The associated variables of adverse outcome were determined using the stepwise multivariable Cox proportional hazards model. Variables with $P < 0.10$ in univariable analysis were included as cofactors for the Cox adjustment. Statistical analyses were performed using SPSS (IBM SPSS Inc., Armonk, NY, USA) and Prism (GraphPad software Inc., San Diego, CA, USA). Differences with a two-tailed P-value < 0.05 were considered significant.

Results

Baseline Characteristics

Among the 247 patients with HCM, 90 (36.4%) were classified as normal weight (average BMI, 20.8 ± 1.7 kg/m^2), 58 (23.4%) as overweight (average BMI, 24.1 ± 0.5 kg/m^2), and 99 (40.2%) as obese (average BMI, 27.6 ± 2.1 kg/m^2). Overweight and obese patients were predominately male and had progressively and significantly higher median plasma triglyceride concentration than normal weight patients (normal weight, 1.1 mmol/L [IQR, 0.8–1.6 mmol/L]; overweight, 1.4 mmol/L [IQR, 1.0–2.2 mmol/L]; obesity, 1.6 mmol/L [IQR, 1.1–2.1]). Similarly, the prevalence of hypertension was significantly higher in overweight and obese patients than in normal weight patients (normal weight, 25.6% vs. overweight, 51.7% vs. obese, 44.4%). Despite similar age among the three groups, the prevalence of NYHA class II/III was significantly higher in obese patients than in nonobese patients. Although no statistical significance was observed, obese patients had the highest median plasma concentrations of NT-proBNP among the three groups ($P = 0.428$). The prevalence of LV outflow obstruction (LVOTO) did not differ significantly among the three groups ($P = 0.224$) (Table 1).

Effect of Obesity on LV Function and Geometry

Overweight and obese patients exhibited significantly higher LVEDV, LVESV, LVSV, and LVM than normal-weight patients. However, when corrected for body size, these indices did not significantly differ among the three groups ($P = 0.342$ for indexed LVEDV; $P = 0.139$ for indexed LVESV; $P = 0.520$ for indexed LVSV) except for indexed LVM (normal weight, 72.9 g/m^2 [IQR, 61.8–86.7 g/m^2] vs. overweight, 79.4 g/m^2 [IQR, 60.3–100.3 g/m^2] vs. obesity, 85.9 g/m^2 [IQR, 72.6–103.8 g/m^2]). Meanwhile, obese patients had a significantly higher LVM/EDV ratio than nonobese patients (normal weight, 0.8 [IQR, 0.7–1.0] vs. overweight, 0.8 [IQR, 0.7–1.1] vs. obesity, 1.0 [IQR, 0.8–1.2]), whereas maximum LVWT was not significantly different across groups ($P = 0.123$). Symmetric LVH was significantly more common in obese patients, with 36.4% of them exhibiting this phenotype. LGE was observed in 109 patients (44.1%) of the entire study cohort, but the amount of LGE did not differ among the three groups ($P = 0.989$). More details of MRI findings can be found in Table 2.

Effect of Obesity on LV Mechanics and Adverse Remodeling

The magnitude of LV global longitudinal (normal weight, −10.4% ± 3.3% vs. overweight, −8.8% ± 3.1% vs. obesity, −7.3% ± 2.7%), circumferential (normal weight, −18.3% ± 3.7% vs. overweight, −16.4% ± 4.1% vs. obesity, −15.8% ± 3.4%), and radial PS (normal weight, 31.6% ± 10.6% vs. overweight, 25.8% ± 8.9%

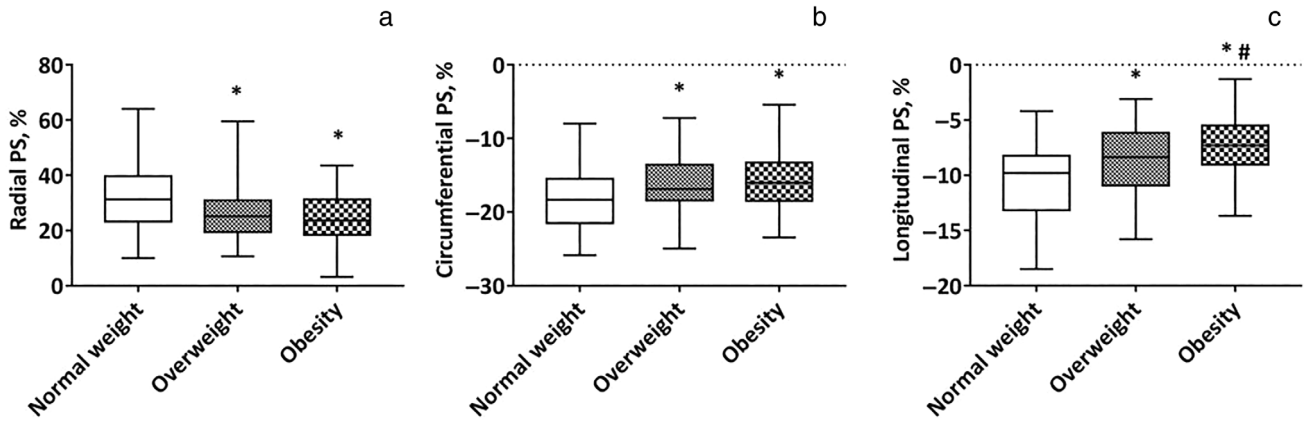

FIGURE 3: Magnitude of global LV systolic strains in the normal weight, overweight, and obese groups. *$P < 0.017$ vs. normal weight cohort. $^{\#}P < 0.017$ vs. overweight cohort. LV, left ventricular; BMI, body mass index; PS, peak strain.

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Linear Regression Analysis of the Determinants of Impaired LV Contractile Function

	Radial PS		Circumferential PS		Longitudinal PS	
	Univariable β	Multivariable β, $R^2 = 0.271$	Univariable β	Multivariable β, $R^2 = 0.228$	Univariable β	Multivariable β, $R^2 = 0.312$
Male	−0.221**		0.127*		0.189**	
BMI						
Overweight[a]	−0.103*	−0.290*	0.195*	0.306*	0.278*	0.313*
Obesity[a]	−0.299*	−0.308**	0.248**	0.392**	0.410**	0.336**
LGE	−0.304**	−0.277**	0.270**	0.295**	0.236**	0.319**
LVOTO	−0.115*		0.119*		0.102*	
Hypertension	−0.013		0.106*		0.118*	

LV, left ventricular; PS, peak strain; BMI, body mass index; LGE, late gadolinium enhancement; LVOTO, left ventricular outflow tract obstruction.
*P-value < 0.05.
**P-value < 0.01.
[a]Normal weight group is the reference group.

Table 4. Linear Regression Analysis of the Determinants of LV Remodeling

	LVMi		LVM/EDV Ratio	
	Univariable β	Muitivariable β, $R^2 = 0.250$	Univariable β	Muitivariable β, $R^2 = 0.191$
Male	0.112		−0.039	
BMI				
Overweight[a]	0.151*	0.186*	0.044	
Obesity[a]	0.288**	0.237**	0.254**	0.188**
LGE	0.253**	0.241**	0.143*	0.142*
LVOTO	0.299**	0.270**	0.213**	0.177**
Hypertension	0.069		0.090	

Abbreviations as in Table 3.
[a]Normal weight group is the reference group.
*P-value < 0.05.
**P-value < 0.01.

vs. obesity, 24.9% ± 8.6%) gradually decreased as BMI class increased (Fig. 3). The radial, circumferential, and longitudinal PS in the overweight and obese subgroups were significantly different from those in the normal weight subgroup. In addition, longitudinal PS in the obese subgroup was significantly different to that in the overweight subgroup. Moreover, the magnitude of BMI was significantly associated with longitudinal ($r = 0.39$), circumferential ($r = 0.32$), and radial PS ($r = -0.33$) (Fig. S1 in the Supplemental Material).

By multivariable linear regression analysis, increased BMI class had a significant association with impaired longitudinal (overweight, $\beta = 0.31$; obesity, $\beta = 0.34$), circumferential (overweight, $\beta = 0.31$; obesity, $\beta = 0.39$), and radial PS (overweight, $\beta = -0.29$; obesity, $\beta = -0.31$) (Table 3). Additionally, the presence of LGE was also associated with impaired strain parameters (longitudinal PS: $\beta = 0.32$; circumferential PS: $\beta = 0.30$; radial PS: $\beta = -0.28$).

Likewise, a similar association was observed when these same analyses were conducted for indexed LVM (overweight,

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

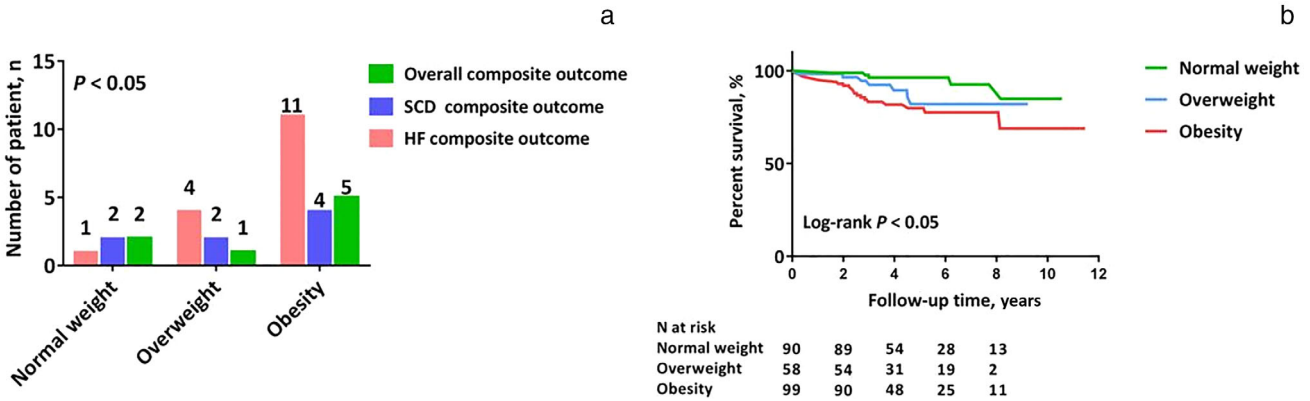

FIGURE 4: Histograms of adverse outcomes among the normal weight, overweight, and obese groups (a) and survival curves (b) during a median follow-up of 4.1 years. SCD, sudden cardiac death; HF, heart failure.

Table 5. Cox Proportional Hazards Regression Analysis to Identify Associated Variables of Adverse Outcomes

	Univariable Analysis		Multivariable Analysis	
	HR (95% CI)	*P*-Value	HR (95% CI)	*P*-Value
LGE	2.87 (1.41–5.83)	0.004	1.81 (1.09–3.97)	0.014
LVOTO	2.81 (1.27–6.21)	0.011	2.39 (1.03–5.58)	0.044
NYHA class III/IV	4.85 (1.22–9.15)	< 0.001	2.87 (1.05–5.78)	0.039
Overweight[#]	3.69 (1.21–7.26)	0.021		
Obesity[#]	4.22 (1.58–7.31)	0.004	3.04 (1.07–6.57)	0.036
Age, per 10 years	1.48 (1.15–1.92)	0.003	1.53 (1.12–2.08)	0.008
Male	1.05 (1.03–2.08)	0.087		

HR, hazards ratio; CI, confidence interval; LGE, late gadolinium enhancement; LVOTO, left ventricular outflow tract obstruction; NYHA, New York Heart Association. # Normal weight group is the reference group.

$\beta = 0.19$; obesity, $\beta = 0.24$) and LVM/EDV ratio (obesity, $\beta = 0.19$) (Table 4). Apart from obesity, the presence of LGE was associated with indexed LVM ($\beta = 0.24$) and LVM/EDV ratio ($\beta = 0.14$). A similar trend was observed for LVOTO when associated with indexed LVM ($\beta = 0.27$) and LVM/EDV ratio ($\beta = 0.18$).

Association Between Obesity and Clinical Outcome

The median follow-up duration for the entire cohort was 4.1 years (IQR, 3.0–6.2 years); During this time frame, 32 patients experienced composite events. The proportion of patients experiencing an adverse event was significantly higher in the obese group than in the normal weight group (20.2% vs. 5.6%). HF composite outcome occurred more frequently in obese patients. Detailed composite event data in the three groups are shown in Fig. 4a. Kaplan–Meier survival analysis revealed that patients with increased BMI class had a significantly higher risk of adverse outcome during follow-up (Fig. 4b). Furthermore, in the multivariable Cox model, obesity remained an independent marker for future adverse events (hazard ratio, 3.04; 95% confidence interval, 1.07–6.57) after adjusting for age, sex, LVOTO, NYHA functional class, and LGE (Table 5).

Discussion

In this study, we investigated the effects of obesity on myocardial mechanics, LV remodeling, and long-term clinical outcomes in Chinese patients with HCM. The main findings were as follows: 1) Obesity was an extrinsic factor that could aggravate LVH. 2) Increased BMI was significantly associated with reduced magnitude of global longitudinal, circumferential, and radial PS. Obese patients exhibited more severe contractile function impairment. 3) During the long-term follow-up, obese patients experienced a higher incidence of adverse outcome than normal weight patients (more than

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3-fold increase). Obesity was independently associated with adverse outcome, irrespective of other factors.

Several studies have demonstrated that LV remodeling occurs because of obesity in the general population. Excessive accumulation of adipose tissue is believed to promote changes in LV morphology via augmentation of cardiac output, chamber enlargement, and ventricular hypertrophy.[13–16] In patients with HCM, obesity may serve as an important environmental regulator, which affects HCM phenotype.[2] However, supporting evidence for this is limited. Olivotto et al reported increased LVM and higher SV in obese patients, but this comparison did not take the body size into consideration.[7] When corrected for body size, we found these indices were comparable among the three BMI classes except for indexed LVM. This indicates that obesity contributes to LV remodeling through mechanisms including and in addition to cardiac output augmentation. Moreover, our data further showed that obesity is an important extrinsic factor for LV phenotype in HCM patients. Obesity may mediate HCM phenotype by other pathways such as sympathetic or neurohormonal activation.[3]

This study indicated that LGE was associated with LV systolic impairment. LGE has been verified as a promising imaging marker for risk stratification in patients with HCM.[17] However, whether obesity aggravates myocardial fibrosis in HCM remains controversial.[4,7] In this study, we found no significant difference with respect to the amount of LGE among subsets of patients with different BMI classes. Since LGE is an important imaging marker with prognostic value and is an indicator of ventricular dysfunction and remodeling, further studies are needed to clarify this issue.[18] Moreover, we observed that maximum LVWT was not affected by body weight, which is consistent with the findings reported by Olivotto et al.[7] Although we acknowledge the importance of LGE burden and maximum LVWT in assessing the severity of disease profile, other imaging markers, such as LVM, cannot be ignored when considering the environmental influence on the HCM phenotype. It has already been reported that obstructive HCM patients have increased LVM while nonobstructive HCM patients may have normal LVM.[9] In this study, LVOTO was associated with increased LVM beside obesity, which indicated that both LVOTO and obesity could influence LVM.

This study also used strain analyses derived from MRI feature tracking to examine LV mechanics in patients with HCM with different BMI classifications. As BMI class increased, LV mechanics exhibited more severe impairment, even though LVEF remained in the normal range. Furthermore, we showed BMI class was associated with the magnitude of strain indices, and degree of LV remodeling. These findings indicate that LV wall stress fails to maintain pace with myocardial hypertrophy during the progression of obesity-triggered LV remodeling, leading to a subtle LV systolic dysfunction.[19] This may in turn explain the profile of a higher risk of HF in obese patients with HCM.[20]

Our data also showed that a higher proportion of obese patients experienced long-term adverse events than nonobese patients. Moreover, we demonstrated that obesity conveys a more than 3-fold increase in risk of future adverse events. Reasons for obesity in patients with HCM have been previously presented by the National Health and Nutrition Examination Survey, which reported that patients with HCM engage in less physical activity at work and leisure to prevent SCD.[5] Although ICD use effectively protects patients with high-risk HCM from SCD, most patients still have negative emotions related to the diagnosis that may result in a less active lifestyle.[8,21,22] Our study further confirmed that obesity in turn contributes to adverse cardiovascular outcomes, particularly HF composite outcome. Thus, exercise training may provide potential benefits for patients with HCM. However, patients with painful and painless myocardial ischemia could exhibit elevated levels of high-sensitive cardiac troponin T (hs-cTnT), which is a biomarker for adverse clinical outcomes; thus, checking hs-cTnT level before exercise training and including only troponin-negative patients is necessary.[23]

Limitations

First, since Asian populations seem to have a higher risk of cardiovascular disease at BMI lower than the established overweight and obesity cutoffs, we used criteria specific for Asians to classify our patients.[3,24] Nonetheless, regardless of the difference in classification criteria due to ethnic background, we found that obesity was related to LV remodeling and adverse outcomes in patients with HCM. Second, genotypic characteristics were not available in this study. However, we demonstrated no significant differences among BMI classes with respect to important phenotypic features that are considered to be affected by genes, such as maximum LVWT and presence of LGE.[7] In addition, a previous study also showed a lack of phenotypic differences between patients with mutations in two common genes associated with HCM (β-myosin heavy chain vs. β-myosin-binding protein C).[25] Third, obesity is associated with diabetes mellitus which may be responsible for silent myocardial ischemia.[26–28] However, coronary arteriography was not carried out for coronary atherosclerosis assessment in this study. Ischemic heart disease may be a possible nonassessed determinant of LV systolic impairment. It would be interesting to investigate the effects of severity and characteristics of coronary atherosclerosis on myocardial contractility in future studies. Finally, the effects of weight loss and exercise training on cardiac remodeling and clinical course remain unclear. Some physical activity key issues, such as optimal intensity and safety, have not been resolved.[6,29]

Conclusion

Obesity is an important environmental modifier contributing to adverse LV remodeling in Chinese patients with HCM. Obese patients exhibit a greater deterioration in myocardial

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

contractile function and have a greater propensity for adverse clinical outcomes, particularly HF or HF-related death, than nonobese patients.

Acknowledgments

This study was financially supported by the 1–3–5 project for disciplines of excellence of West China Hospital, Sichuan University (ZYGD18013).

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Baxi AJ, Restrepo CS, Vargas D, Marmol-Velez A, Ocazionez D, Murillo H. Hypertrophic cardiomyopathy from A to Z: Genetics, pathophysiology, imaging, and management. Radiographics 2016;36(2):335-354.
2. Finocchiaro G, Magavern E, Sinagra G, et al. Impact of demographic features, lifestyle, and comorbidities on the clinical expression of hypertrophic cardiomyopathy. J Am Heart Assoc 2017;6(12):e007161.
3. Badimon L, Bugiardini R, Cenko E, et al. Position paper of the European Society of Cardiology-working group of coronary pathophysiology and microcirculation: Obesity and heart disease. Eur Heart J 2017;38(25):1951-1958.
4. Neubauer S, Kolm P, Ho CY, et al. Distinct subgroups in hypertrophic cardiomyopathy in the NHLBI HCM registry. J Am Coll Cardiol 2019;74(19):2333-2345.
5. Reineck E, Rolston B, Bragg-Gresham JL, et al. Physical activity and other health behaviors in adults with hypertrophic cardiomyopathy. Am J Cardiol 2013;111(7):1034-1039.
6. Saberi S, Day SM. Exercise and hypertrophic cardiomyopathy: Time for a change of heart. Circulation 2018;137(5):419-421.
7. Olivotto I, Maron BJ, Tomberli B, et al. Obesity and its association to phenotype and clinical course in hypertrophic cardiomyopathy. J Am Coll Cardiol 2013;62(5):449-457.
8. Fumagalli C, Maurizi N, Day SM, et al. Association of obesity with adverse long-term outcomes in hypertrophic cardiomyopathy. JAMA Cardiol 2020;5(1):65-72.
9. Authors/Task Force Members, Elliott PM, Anastasakis A, et al. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: The task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014;35(39):2733-2779.
10. Avanesov M, Münch J, Weinrich J, et al. Prediction of the estimated 5-year risk of sudden cardiac death and syncope or non-sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy using late gadolinium enhancement and extracellular volume CMR. Eur Radiol 2017;27(12):5136-5145.
11. Yang L, Zhang L, Cao S, et al. Advanced myocardial characterization in hypertrophic cardiomyopathy: Feasibility of CMR-based feature tracking strain analysis in a case-control study. Eur Radiol 2020;30(11):6118-6128.
12. Peng WL, Zhang TJ, Shi K, et al. Automatic machine learning based on native T1 mapping can identify myocardial fibrosis in patients with hypertrophic cardiomyopathy. Eur Radiol 2022;32(2):1044-1053.
13. Wong CY, O'Moore-Sullivan T, Leano R, Byrne N, Beller E, Marwick TH. Alterations of left ventricular myocardial characteristics associated with obesity. Circulation 2004;110(19):3081-3087.
14. Abel ED, Litwin SE, Sweeney G. Cardiac remodeling in obesity. Physiol Rev 2008;88(2):389-419.
15. Alpert MA, Lavie CJ, Agrawal H, Aggarwal KB, Kumar SA. Obesity and heart failure: Epidemiology, pathophysiology, clinical manifestations, and management. Transl Res 2014;164(4):345-356.
16. Alpert MA, Omran J, Bostick BP. Effects of obesity on cardiovascular hemodynamics, cardiac morphology, and ventricular function. Curr Obes Rep 2016;5(4):424-434.
17. Mentias A, Raeisi-Giglou P, Smedira NG, et al. Late gadolinium enhancement in patients with hypertrophic cardiomyopathy and preserved systolic function. J Am Coll Cardiol 2018;72(8):857-870.
18. Weng Z, Yao J, Chan RH, et al. Prognostic value of LGE-CMR in HCM: A meta-analysis. JACC Cardiovasc Imaging 2016;9(12):1392-1402.
19. Lavie CJ, Pandey A, Lau DH, Alpert MA, Sanders P. Obesity and atrial fibrillation prevalence, pathogenesis, and prognosis: Effects of weight loss and exercise. J Am Coll Cardiol 2017;70(16):2022-2035.
20. Hinojar R, Fernández-Golfín C, González-Gómez A, et al. Prognostic implications of global myocardial mechanics in hypertrophic cardiomyopathy by cardiovascular magnetic resonance feature tracking. Relations to left ventricular hypertrophy and fibrosis. Int J Cardiol 2017;249:467-472.
21. Maron BJ, Casey SA, Olivotto I, et al. Clinical course and quality of life in high-risk patients with hypertrophic cardiomyopathy and implantable cardioverter-defibrillators. Circ Arrhythm Electrophysiol 2018;11(4):e005820.
22. Maron MS, Rowin EJ, Wessler BS, et al. Enhanced American College of Cardiology/American Heart Association strategy for prevention of sudden cardiac death in high-risk patients with hypertrophic cardiomyopathy. JAMA Cardiol 2019;4(7):644-657.
23. Liao H, Tan HC, Wang Z, Chen X, He Y, He S. Combined evaluation of coronary artery disease and high-sensitivity cardiac troponin T for prediction of adverse events in patients with hypertrophic cardiomyopathy. BMC Cardiovasc Disord 2021;21(1):325.
24. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363(9403):157-163.
25. Weissler-Snir A, Hindieh W, Gruner C, et al. Lack of phenotypic differences by cardiovascular magnetic resonance imaging in MYH7 (β-myosin heavy chain)- versus MYBPC3 (myosin-binding protein C)-related hypertrophic cardiomyopathy. Circ Cardiovasc Imaging 2017;10(2):e005311.
26. Paolisso P, Foà A, Bergamaschi L, et al. Hyperglycemia, inflammatory response and infarct size in obstructive acute myocardial infarction and MINOCA. Cardiovasc Diabetol 2021;20(1):33.
27. Sala L, Pontiroli AE. Role of obesity and hypertension in the incidence of atrial fibrillation, ischaemic heart disease and heart failure in patients with diabetes. Cardiovasc Diabetol 2021;20(1):162.
28. Jiang L, Shi K, Guo YK, et al. The additive effects of obesity on myocardial microcirculation in diabetic individuals: A cardiac magnetic resonance first-pass perfusion study. Cardiovasc Diabetol 2020;19(1):52.
29. Bendor CD, Bardugo A, Pinhas-Hamiel O, Afek A, Twig G. Cardiovascular morbidity, diabetes and cancer risk among children and adolescents with severe obesity. Cardiovasc Diabetol 2020;19(1):79.

15222586, 2023, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/jmri.28306 by Indian Institute Of Technology, Wiley Online Library on [10/11/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License