Original Article

Quadratic stratification of left ventricular hypertrophy and association with mitral insufficiency grading: a retrospective study using cardiac magnetic resonance

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Background: Chronic primary mitral regurgitation (MR) is caused by the defect in >1 component of the mitral valve, potentially leading to left ventricular hypertrophy (LVH). The relationship between LVH subtypes and the insufficiency grading of chronic MR remains unclear. Thus, we aimed to investigate this association and explore the impact of unhealthy habits on LVH development in patients with chronic primary MR through a cross-sectional study.

Methods: Cardiac magnetic resonance (CMR) data was retrospectively collected from 3T magnetic resonance imaging (MRI) scanners in 71 patients with chronic primary MR (range, 20–84 years, 52% men). Considered patients (with mild-to-severe MR) were enrolled between March 2015 and September 2022 from the Cardiovascular Imaging Registry of Calgary (CIROC) database. Left ventricle (LV) function was assessed using cvi42 v5.11.5. Patients were categorized into 'mild-to-severe' MR using regurgitation fraction (RF), according to the current imaging guidelines. LVH subtypes were determined using mass-to-volume (M/V) calculations. IBM SPSS was used to run all the statistical analyses. This study employed normality checks by using the Shapiro-Wilk test; one-way analysis of variance (ANOVA) and Kruskal-Wallis tests with post-hoc pairwise comparisons; Chi-squared tests, Fisher's Exact test, crosstabulation analysis, and multinomial logistic regression to examine relationships between MR severity, LVH types, and impact of lifestyle factors, significance at $P<0.05$.

Results: Eccentric LVH was significantly associated with increased severity of MR, while concentric remodeling (CR) was linked to decreased MR severity (χ^2=13.276, P=0.03, stratified by sex χ^2=7.729, P=0.005). Sex differences emerged in the overall study population. Eccentric LVH was dominantly higher than CR in both males and females (females: 57.7% *vs.* 42.3%, P=0.05, males: 82.8% *vs.* 17.2%, P=0.26). No differences were observed between age groups ('Young-Middle' = under 60 years, and 'Middle-Old' = over 60 years). Still, there were notable differences in LVH prevalence within the 'Young-Middle' age group for mild-moderate (P=0.01) and moderate-severe MR (P=0.02). Eccentric LVH was associated with higher body mass index (BMI), smoking, and frequent alcohol consumption [odds ratio (OR) 1.02, 95% confidence interval (CI): 0.56–1.26; OR 1.65, 95% CI: 1.31–6.52; OR 1.15, 95% CI: 0.26–1.34], while CR was solely

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associated with increased BMI (smokers OR =1.84, 95% CI: 1.25–3.91 and alcohol consumers OR =1.32, 95% CI: 0.86–2.48). Nicotine and caffeine consumption did not appear to be a risk factor for LVH (nicotine: eccentric, OR =0.99, 95% CI: 0.65–1.86; CR, OR =0.97, 95% CI: 0.69–2.39 and caffeine: eccentric, OR =0.69, 95% CI: 0.48–1.61; CR, OR =0.97, 95% CI: 0.78–4.01).

Conclusions: This study reveals sex-based associations between LVH subtypes and severity of chronic primary MR. Lifestyle factors such as cigarette smoking, alcohol consumption, and elevated BMI influence LVH risk, while nicotine and caffeine consumption exhibit minimal effects.

Keywords: Cardiovascular disease; left ventricular hypertrophy (LVH); quadratic classification; mitral regurgitation (MR); cardiac magnetic resonance (CMR)

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Introduction

Background

Valvular heart disease (VHD) affects around 2.5–3% of the world's population and the prevalence increases as people age (1). In developed countries, mitral regurgitation (MR) is the most common type of VHD. MR is characterized by systolic retrograde blood flow from the left ventricle (LV) into the left atrium (LA), a frequently cited reason for valve surgery (2). Therefore, early detection and assessment of MR are crucial (3). MR is generally classified as acute and chronic. The disruption of different parts of the mitral valve apparatus causes acute MR. Chronic MR is further classified into chronic primary MR (degenerative) and chronic secondary (functional) MR (4). In chronic primary MR, the pathology of more than one of the components of the valve (leaflets, chordae tendineae, papillary muscles, annulus) causes valve incompetence (e.g., mitral valve leaflet prolapse), with systolic regurgitation of blood from the LV to the LA. It is predominantly caused by degenerative disease in developed countries, whereas secondary MR is a consequence of other cardiac diseases involving the myocardium [e.g., dilated cardiomyopathy, and myocardial infarction (MI)] (5). On the other hand, left ventricular hypertrophy (LVH) is a condition in which there is an increase in left ventricular mass, either due to an increase in wall thickness, left ventricular cavity enlargement, or both (6). It can be either concentric or eccentric. Concentric LVH denotes an increase in wall thickness and a decrease in chamber volume. Eccentric LVH signifies an increase in both chamber volume and wall thickness. LVH affects more than 15% of the general population. It is denoted as a risk factor for several cardiovascular events, including MR (6). A report by Kawel-Boehm *et al.* indicates that regressing LVH can decrease cardiac events by 59% (7). This highlights the significance of early evaluation of LVH. Echocardiography (doppler) is the primary imaging assessment tool commonly used for both MR and LVH. However, echocardiography has limitations in determining the severity level and post-surgical outcomes (8). Recent studies have shown that cardiac magnetic resonance (CMR) can provide a more accurate depiction of the regurgitant jet and flow patterns overcoming the limitations of echocardiography (1,8). Thus,

Highlight box

Key findings
- Cardiac magnetic resonance (CMR) parameters effectively simplify left ventricular hypertrophy (LVH) classification.
- Distinct associations between LVH types and chronic primary mitral regurgitation (MR) severity, especially across sex types and age groups.
- Introduces insights into age-stratified prevalence patterns and unfolds the impact of unhealthy lifestyles.

What is known and what is new?
- CMR parameters' role in primary MR classification and their general link with LVH.
- LVH classification with CMR parameters, the association between specific MR severity with LVH subtypes, and rules out caffeine or nicotine as LVH risk factors.

What is the implication, and what should change now?
- Improve patient care by simplifying LVH classification and tailoring treatments based on risk factors.
- Enhance care further by implementing CMR training, adopting tailored protocols, and prioritizing interventions.

we utilized CMR to classify both MR and LVH precisely.

Rationale and knowledge gap

Previous studies emphasized the general relationship between primary MR and LVH (9-12). However, it is still uncertain whether a specific type of LVH (eccentric or concentric) is linked to a certain MR severity grading which serves as a potential gap. Surgical repair or replacement of the mitral valve is currently the only recommended therapy for severe chronic primary MR (9). The chronic elevation of wall stress caused by the resulting volume overload leads to structural remodeling and it may lead to heart failure (HF) if it stands long (13). To prevent the development of LVH in patients with primary MR, it is necessary to understand the impact of severity grading.

Objective

Previous investigations have only established a general association, and most studies used echocardiography (10,11). Thus, our study aims to investigate this unexplored relationship using CMR as the imaging modality. Our study hypothesized that severe chronic primary MR is associated with eccentric LVH, as severity increases the chamber volume and, therefore, eccentric LVH. Furthermore, research has shown that unhealthy lifestyle choices increase the risk of developing cardiovascular diseases (14). Nevertheless, the effects of combining lifestyle choices with body mass index (BMI), sex, and persistent MR remain unclear. Therefore, we further explored and unfolded the impact of unhealthy lifestyle choices on developing specific types of LVH. We hypothesized that an unhealthy lifestyle is a major risk factor for LVH in mitral patients influenced by BMI. We tested our hypothesis via a sex and age-based retrospective cross-sectional study. We present the article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-466/rc).

Methods

Study design

This study employed a retrospective cross-sectional study design to examine the relationship between the specific types of LVH and MR severity grading. The data were acquired at a single point in time without longitudinal follow-up.

Study population

The initial study population from the Cardiovascular Imaging Registry of Calgary (CIROC) database was n=25,107. The inclusion criteria were any patients referred for the assessment of heart valve disease with a native mitral valve (n=118). Then patients (n=47) with none and trivial MR (as defined in section "Mitral insufficiency grading") were excluded as the scope was to assess the effect of mild-severe MR, leading to the overall study population, adult patients (n=71) ranging from 20 to 84 years old. All of them were diagnosed with chronic primary MR and identified with persistent heart disease. CMR was conducted at the Foothills Medical Centre (FMC) to evaluate their condition. A standardized patient-reported health (PRH) questionnaire was used to collect baseline demographic information, inclusive of ethnicity, education level, employment status, comorbid cardiac and non-cardiac diseases, alcohol consumption, smoking history, patient-reported shortness of breath based on the New York Heart Association (NYHA) classification, and quality of life. Participants were selected through convenience sampling, and only those with mild-moderate, moderate, moderate-severe, and severe MR were eligible. BMI groups were classified as 'Underweight' (BMI <18.5 kg/m^2), 'Normal Weight' (BMI 18.5–24.9 kg/m^2), 'Overweight' (BMI 25–29.9 kg/m^2), and 'Obesity' (BMI ≥30 kg/m^2) (15). A flow diagram describing the entire flow from screening to the final inclusion of patients is demonstrated in *Figure 1*.

Ethics and registry

Data from patients were provided by the CIROC (NCT04367220). CIROC is a clinical outcomes registry of the Libin Cardiovascular Institute routinely engaging patients referred to cardiac imaging services in Southern Alberta. Patients provided informed consent for data usage and completed standardized patient health questionnaires at the time of testing. All imaging studies were protocolled using commercial software (cardioDITM, Cohesic Inc., Calgary, Canada). Patients enrolled between March 2015 and September 2022 were considered in this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Conjoint Health Research Ethics Board at the

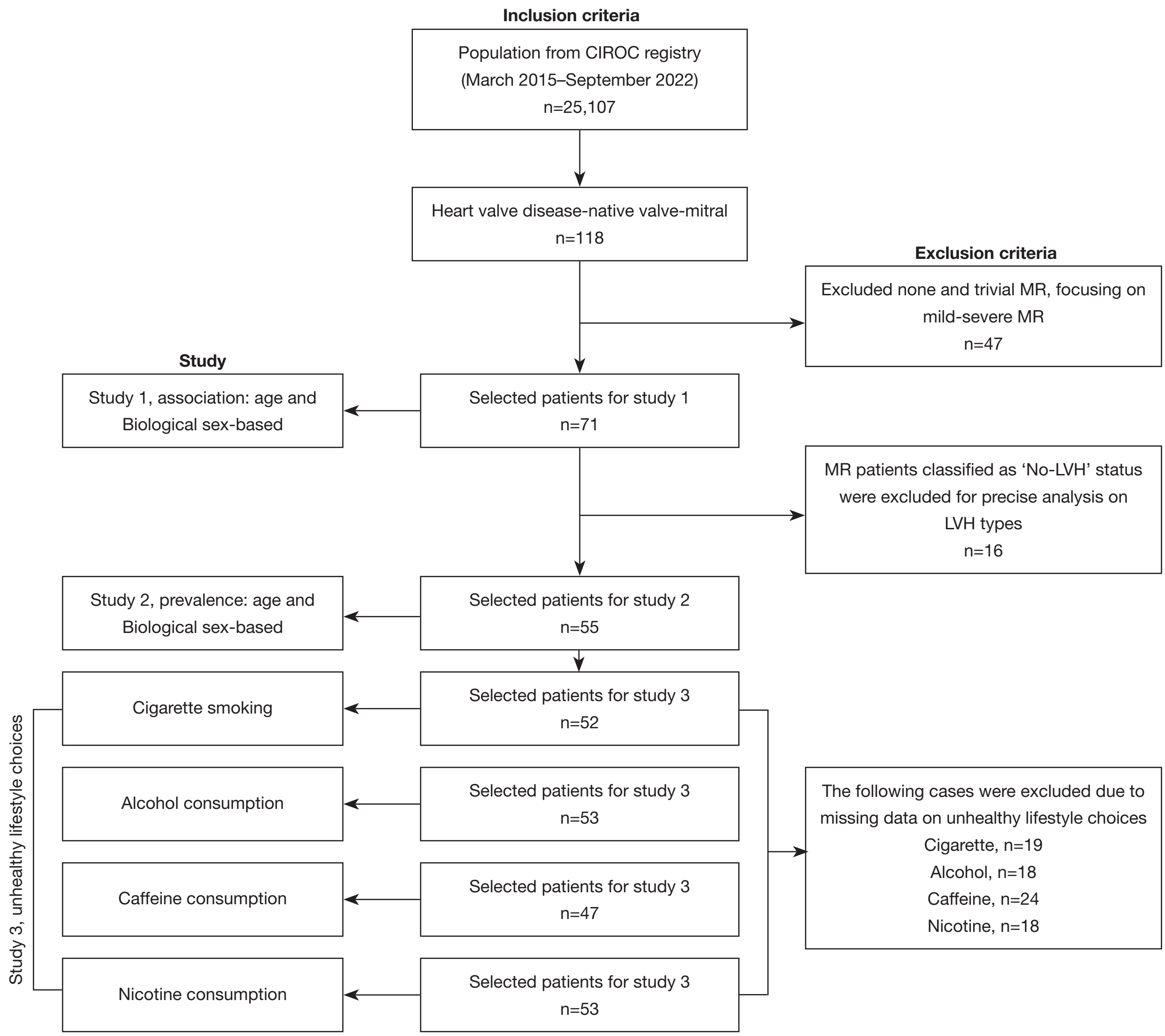

Figure 1 Flow diagram of study population detailing inclusion and exclusion criteria. CIROC, Cardiovascular Imaging Registry of Calgary; MR, mitral regurgitation; LVH, left ventricular hypertrophy.

University of Calgary (REB#13-0902) and informed consent was taken from all the patients.

CMR protocol

All participants underwent a consistent standardized imaging protocol using 3 Tesla magnetic resonance imaging (MRI) scanners (Skyra, Prisma, Siemens, Erlangen, Germany). Multi-planar segmented electrocardiogram (ECG) gated, time-resolved balanced steady-state free precession (SSFP) cine imaging was conducted in four-chamber, three-chamber, two-chamber, and short-axis views to assess the left ventricular function. The two-dimensional phase contrast (2D PC) data was acquired over multiple cardiac cycles using ECG-gated cine imaging to measure time-resolved pulsatile blood flow. The 2D imaging slice was positioned normal to the vessel lumen. Data acquisition included single-direction velocity measurement orthogonal to the 2D imaging slice (through-plane encoding) and was performed during a 10–20-second breath-hold period. Following image reconstruction, 2D cine PC-MRI yields a series of anatomical (magnitude) and flow velocity (phase

Table 1 CMR parameters associated with chronic primary MR severity grading

Parameters	Mitral severity			
	Mild-moderate	Moderate	Moderate-severe	Severe
LVEF (%)	Normal-mildly reduced [50–70]	Normal-mildly reduced [40–49]	Mild-moderately reduced [30–39]	Severely reduced [<30]
RV (mL)	10–29	30–59	60–79	≥80
RF (%)	≤15	16–25	26–48	≥49
LVEDV	Normal or slightly increased	Moderately increased	Significantly increased	Significantly increased

CMR, cardiac magnetic resonance; MR, mitral regurgitation; LVEF, left ventricle ejection fraction; RV, regurgitation volume; RF, regurgitation fraction; LVEDV, left ventricle end-diastolic volume.

difference) images that represent the temporal changes of morphology and blood flow over the cardiac cycle. The typical measurement parameters were velocity encoding (VENC) =150 m/s, spatial resolution =1.5–2.5 mm/pixel, temporal resolution =30–60 ms, and slice thickness =5–8 mm, cardiac phase =30.

Post processing

All the post-processing was done using the cvi42 software. Cine SSFP short-axis images were analyzed regarding the calculation of LV function. Endo- and epicardial borders were contoured manually in short-axis (SAX) cine images at end-diastole and end-systole. The basal slice was included in the analysis if at least 50% of blood volume was surrounded by myocardium. Papillary muscles were excluded and considered part of the blood pool. Ejection fraction (EF, %), myocardial mass (Mass, g), end-systolic volume, and end-diastolic volume (ESV and EDV, mL) were recorded as LV function (16,17). The 2D PC MRI images were evaluated for forward stroke volume (SV). Postprocessing required the definition of vessel contour in all phases and the application of background correction. The ascending aorta was contoured in the magnitude image with the sharpest blood/tissue contrast. Contours were propagated to phase contrast images in all temporal phases and corrected manually. The background correction was conducted by defining a flow-free area. This correction was then applied to all phases, followed by baseline correction selection. The forward SV (mL) was calculated automatically in all phases (18). The mitral regurgitant volume was calculated by subtracting aortic forward flow volume (AoPC) from LV stroke volume (LVSV); where LV stroke volume = left ventricular end-diastolic volume (LVEDV) – left ventricular end-systolic volume (LVESV) (2,19,20). Finally, the regurgitation fraction (RF) was calculated by using the formula: RF = [regurgitant volume/(forward flow volume + regurgitant volume)] × 100% (21). The EF was calculated from EDV and ESV estimates, using the following formula: EF = (EDV – ESV)/EDV (22).

Mitral insufficiency grading

The degree of mitral severity was assessed using the guidelines set by the American College of Cardiology and American Heart Association (ACC and AHA) following the grading criteria A–D for chronic primary MR (4,22). *Table 1* illustrates the corresponding cut-off ranges of CMR parameters for mild-moderate, moderate, moderate-severe, and severe MR (22,23). The primary marker for the evaluation was RF% (24). *Table 1* illustrates the cut-off ranges of EF severity, which is a powerful parameter in detecting VHD (4,22).

Quadratic classification of LVH

The study was conducted on chronic primary MR patients diagnosed with mild-moderate to severe MR. The standard LVH classification by echocardiography utilizes the relative wall thickness (RWT) and LV mass indexed (LVMI) (25). This study classified LV remodeling into four categories using LVMI and left ventricular end-diastolic volume indexed (LVEDVI) by CMR instead of the standard echocardiographic (Echo) classification. For the no LVH category, LVEDVI ranges were 55–96 mL/m^2 for females and 57–105 mL/m^2 for males. Concentric LVH, eccentric LVH, and concentric remodeling (CR) were categorized with normal or slightly decreased LVEDVI (females ≤80 mL/m^2, males ≤85 mL/m^2), increased LVEDVI (females ≥96 mL/m^2, males ≥105 mL/m^2), and normal or

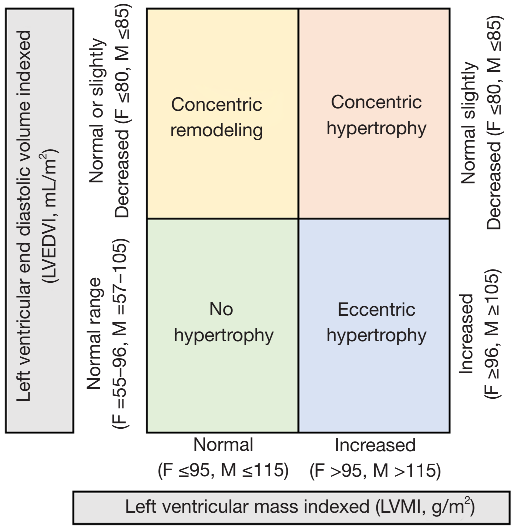

Figure 2 Ranges of left ventricular function for quadratic classification of LVH. F, female; M, male; LVH, left ventricular hypertrophy.

slightly decreased LVEDVI (females ≤80 mL/m^2, males ≤85 mL/m^2), respectively (25-27). LVMI ranges for no LVH, and CR were ≤115 g/m^2 for males and ≤95 g/m^2 for females. LVMI ranges for concentric and eccentric LVH were LVMI >115 g/m^2 for males and LVMI >95 g/m^2 for females (22). *Figure 2* provides the ranges of LVEDVI and LVMI for no hypertrophy, concentric LVH, eccentric LVH, and CR.

Statistical analysis

The IBM SPSS Statistics for Windows Version 26 software (IBM Corp., Armonk, NY, USA) was used for all the statistical analysis. A visual representation by histogram and Shapiro-Wilk test was conducted to ensure the normality of the data. Among the presented parameters, systolic blood pressure (SBP), diastolic blood pressure (DBP), body surface area (BSA), LV mass (LVM) and RF showed normal distribution, while others did not. A one-way analysis of variance (ANOVA) test was used for normally distributed data to determine any significant differences within the hemodynamic parameters presented among the MR severity groups. For non-normally distributed data, the Kruskal-Wallis test was conducted. An additional pairwise comparison was done to identify any significant differences among the MR severity groups. The association between mitral severity and each LVH type was assessed using the Chi-squared test of independence, Fisher's Exact, and Crosstabulation analysis. The prevalence of LVH was determined using the Chi-squared test of independence. Age and sex were used as stratification variables. Multinomial logistic regression was used to examine the impact of unhealthy lifestyle factors and the risk of developing a specific type of LVH. Smoking cigarettes, and consumption of alcohol, caffeine, and nicotine were considered independent variables. The BMI and sex were used as the covariant variables for this analysis. All assumptions such as the test of independence, sample size, and types of variables were met before running the non-parametric statistical tests. The reported P values are two-sided and P value <0.05 was considered statistically significant.

Results

Table 2 demonstrates the baseline characteristics of the study population across different severity categories (mild-moderate, moderate, moderate-severe, and severe). More males than females were found in certain severity groups (mild-moderate: eight males *vs.* seven females, moderate-severe: nine males *vs.* five females, and severe: six males *vs.* four females, this study considered the biological sex). *Table 3* comprises of LV function of the patients. The general characteristics include age (years), height (cm), weight (kg), heart rate (HR, beats/min), SBP (mmHg), DBP (mmHg), BMI (kg/m^2), and BSA (m^2). The cardiac LV function consists of LVMI (g/m^2), LVM (g/m^2), LVEDVI (mL/m^2), LVEDV (mL/m^2), left ventricular end-systolic volume indexed (LVESVI, mL/m^2), LVESV (mL/m^2), and left ventricular ejection fraction (LVEF, %). The LVM, LVEDV, LVESV, and BMI were indexed by BSA. The RF (%) is also presented among severity grades. The normally distributed continuous data is shown via mean ± standard deviation (SD) and the non-normally distributed data is represented by the median [interquartile range (IQR)]. The LVEDVI, LVEDV, and RF showed notable differences within MR severity groups (P=0.003, P=0.006, P<0.001, respectively). Significant differences were observed when comparing mild-moderate to moderate-severe (LVEDVI: P=0.01, LVEDV: P=0.02, RF: P<0.001), mild-moderate to severe (LVEDVI: P=0.003, LVEDV: P=0.002, RF: P<0.001), moderate to moderate-severe (LVEDVI: P=0.03, LVEDV: P=0.01, RF: P<0.001), and moderate to severe (LVEDVI: P=0.007, RF: P<0.001).

Table 2 Baseline characteristics

Demographics and clinical characteristics	Mitral insufficiency grade				
	Mild-moderate (n=15)	Moderate (n=32)	Moderate-severe (n=14)	Severe (n=10)	P value
Sex					–
Male	8	14	9	6	
Female	7	18	5	4	
Age (years)	64 [18]	53.5 [19]	65 [17]	52 [19]	0.18
Height (cm)	168 [14]	168 [11.25]	169 [18]	177.5 [20.75]	0.53
Weight (kg)	78 [9]	76 [25]	75.5 [18]	75.5 [20]	0.98
HR (beats/min)	69 [22]	73.5 [16]	67 [24]	68 [15]	0.61
SBP (mmHg)	124.87±17.2	114.22±16.92	118.07±15.9	113.4±13.01	0.18
DBP (mmHg)	72.2±13.9	71.25±13.9	72.36±9.96	70.3±8.17	0.97
BSA (m^2)	1.86±0.22	1.88±0.22	1.88±0.18	1.89±0.23	0.97
BMI (kg/m^2)	27.04 [5.58]	29.06 [13.10]	25.88 [4.32]	24.56 [5.04]	0.91

Values are n, mean ± SD, and median [IQR]. Non-commercial and no derive reuse with exemptions from licenses of the *Journal of Cardiovascular Magnetic Resonance* under the journal's copyright policy CC BY-NC-ND https://s100.copyright.com/AppDispatchServlet?publisherName=ELS&contentID=S1097664724007476&orderBeanReset=true. Source: Monisha Srabanti, Julio Garcia. Kiosk 6R-TA-11 - Quadratic Stratification of Left Ventricular Hypertrophy and Relationship with Mitral Insufficiency Grading: A Retrospective Study Using Cardiac Magnetic Resonance. *Journal of Cardiovascular Magnetic Resonance*. 2024;26(Supplement 1):100756. HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; BSA, body surface area; BMI, body mass index; SD, standard deviation; IQR, interquartile range.

Table 3 Cardiac left ventricular function

Ventricular function	Mitral insufficiency grade				
	Mild-moderate (n=15)	Moderate (n=32)	Moderate-severe (n=14)	Severe (n=10)	P value
LVMI (g/m^2)	58.95 [10]	58.25 [29.9]	70 [33.1]	69.1 [32.6]	0.08
LVM (g/m^2)	119.86±36.5	120.4±39.17	133.5±31.78	145.2±30.03	0.21
LVEDVI (mL/m^2)	81.85 [32.6]†‡	96.2 [58.5]§¶	112 [58.4]†§	144.8 [38.8]‡¶	0.003*
LVEDV (mL/m^2)	157.5 [33.75]†‡	181 [131.5]§¶	239 [100]†§	253 [91]‡¶	0.006*
LVESVI (mL/m^2)	32.75 [11.6]	45.95 [66]	49.6 [82.9]	50.7 [91.4]	0.21
LVESV (mL/m^2)	56.5 [19.75]	89 [113.5]	93 [137]	100 [125]	0.12
LVEF (%)	61.9 [6.5]	51.15 [29.6]	46.2 [37.6]	52.6 [37.3]	0.87
RF (%)	24.73±6.1†‡	30.75±6.910§¶	48.43±9.95†§	56.4±8.98‡¶	<0.001*

Values are mean ± SD and median [IQR], *, P value <0.05 was considered statistically significant. †, P value <0.05 for mild-moderate versus moderate-severe, ‡, P value <0.05 for mild-moderate versus severe, §, P value <0.05 for moderate versus moderate-severe, ¶, P value <0.05 for moderate versus severe. Non-commercial and no derive reuse with exemptions from licenses of the *Journal of Cardiovascular Magnetic Resonance* under the journal's copyright policy CC BY-NC-ND https://s100.copyright.com/AppDispatchServlet?publisherName=ELS&contentID=S1097664724007476&orderBeanReset=true. Source: Monisha Srabanti, Julio Garcia. Kiosk 6R-TA-11 - Quadratic Stratification of Left Ventricular Hypertrophy and Relationship with Mitral Insufficiency Grading: A Retrospective Study Using Cardiac Magnetic Resonance. *Journal of Cardiovascular Magnetic Resonance*. 2024;26(Supplement 1):100756. LVMI, left ventricle mass indexed; LVM, left ventricle mass; LVEDVI, left ventricle end-diastolic volume indexed; LVEDV, left ventricle end-diastolic volume; LVESVI, left ventricle end-systolic volume indexed; LVESV, left ventricle end-systolic volume; LVEF, left ventricle ejection fraction; RF, regurgitation fraction; SD, standard deviation; IQR, interquartile range.

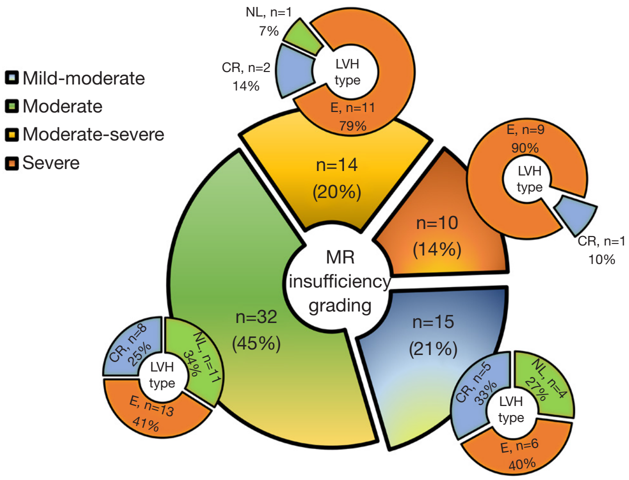

Figure 3 Categorization of the study population. LVH, left ventricular hypertrophy; MR, mitral regurgitation; CR, concentric remodeling; NL, no LVH; E, eccentric.

Among the 71 patients with chronic primary MR, n=15 (21%) were classified as mild-moderate, n=32 (45%) as moderate, n=14 (20%) as moderate-severe, and n=10 (14%) as severe MR. The mild-moderate severity level was sub-categorized into no LVH, n=4 (27%), eccentric LVH, n=6 (40%), and CR, n=5 (33%). Similarly, moderate MR was sub-classified into no LVH, n=11 (34%), eccentric LVH, n=13 (41%), and CR, n=8 (25%). The moderate-severe MR was sub-classified into no LVH, n=1 (7%), eccentric LVH, n=11 (79%), and CR, n=2 (14%). Finally, severe MR was sub-classified into eccentric LVH, n=9 (90%), and CR, n=1 (10%). The sub-classification of LVH was done using the ranges of LV function illustrated in *Figure 2*. *Figure 3* illustrates the categorization of 71 cases into four grades of MR insufficiency, each further subdivided into types of LVH. *Figure 4* shows the left ventricular SAX views from cine images (end-diastolic phase) for each LVH condition

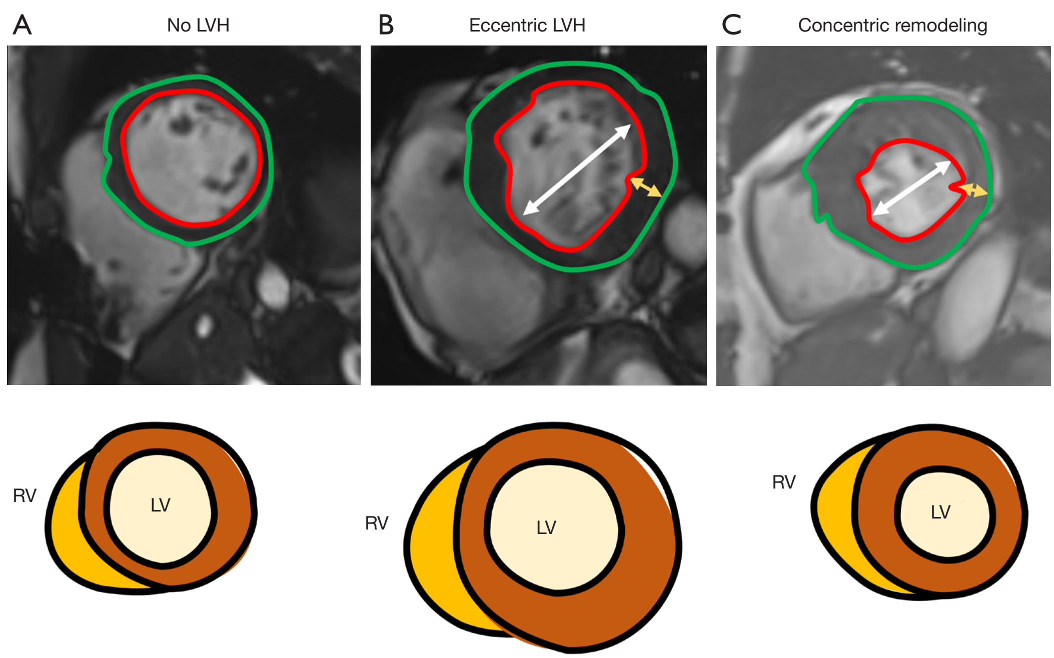

Figure 4 Left ventricular SAX views in the end-diastolic phase for LVH conditions. (A) Shows the no LVH condition in a 49-year-old female patient with mild-moderate chronic primary MR (LVM and LVEDV = normal); (B) shows the eccentric LVH condition in a 53-year-old male patient with moderate chronic primary MR (LVM and LVEDV = increased); (C) shows the concentric remodeling condition in a 60-year-old female patient with severe chronic primary MR (LVM = normal, LVEDV = reduced). Red circle indicates endocardium of left ventricle; green circle indicates epicardium of left ventricle; white arrow indicates left ventricle diameter (demonstrating increased or decreased left ventricle volume); yellow arrow indicates left ventricle wall thickness (demonstrating increased or decreased left ventricle mass). LVH, left ventricular hypertrophy; RV, right ventricle; LV, left ventricle; SAX, short-axis; MR, mitral regurgitation; LVM, left ventricle mass; LVEDV, left ventricle end-diastolic volume.

classified by CMR. *Figure 4A* shows the no LVH condition in a 49-year-old female patient with mild-moderate chronic primary MR (LVM and LVEDV = normal); *Figure 4B* shows the eccentric LVH condition in a 53-year-old male patient with moderate chronic primary MR (LVM and LVEDV = increased) and *Figure 4C* shows the CR condition in a 60-year-old female patient with severe chronic primary MR (LVM = normal, LVEDV = reduced). The yellow arrow demonstrates the LV wall thickness, and the white arrow demonstrates the LV chamber dimension (LV volume).

Relationship between chronic primary MR severity and each type of LVH (stratified by sex and age)

A strong association was observed between the categories of LVH (no LVH, eccentric, CR) and chronic primary MR severity grading (mild-moderate, moderate, moderate-severe, and severe). Eccentric LVH exhibited a significant association with severe MR and demonstrated a stronger association with moderate-severe MR. Conversely, CR was strongly associated with mild-moderate MR. *Figure 5A* visually depicts an increasing association between eccentric LVH and higher MR severity grades (R^2=0.90), while a descending trend was observed with CR (R^2=0.97). These findings provide robust evidence of an association between chronic primary MR severity grading and the type of LVH (Pearson's Chi-squared test, χ^2=13.276, df=6, P=0.03). Similarly, the likelihood ratio test value (χ^2=15.579, df=6, P=0.02), and Fisher's Exact test value (χ^2=12.354, df=6, P=0.04), further supported a significant association.

The crosstabulation analysis revealed a significant association between LVH type and severity of chronic primary MR, stratified by sex (Pearson's Chi-squared test, χ^2=7.729, df=1, P=0.005), which was further supported by the likelihood ratio statistics (χ^2=8.077, df=1, P=0.004). The association was driven by a higher proportion of males with eccentric LVH who had moderate-severe chronic primary MR. Conversely, females with moderate MR showed the highest association with CR. These findings highlight a sex-based difference in the association between these variables (P=0.03). *Figure 5B* illustrates the sex-specific association between LVH and chronic primary MR severity.

There was no significant association between the type of LVH and chronic primary MR severity grading for both the 'Young-Middle' age group (under 60 years old, male =10, female =20) (χ^2=7.015, df=6, P=0.34) and the 'Middle-Old' age group (over 60 years old, male =27, female =14) (χ^2=10.213, df=6, P=0.11). Therefore, there is no indication that LVH type and chronic primary MR severity are more or less likely to appear together in either age group.

Prevalence of LVH among chronic primary MR patients (stratified by sex and age)

For this study, the no LVH category (n=16) was excluded from the total population (n=71) to ensure a precise analysis. The study included a total of 55 patients, with 26 females (47.3%) and 29 males (52.7%). The age groups represented were the 'Young-Middle' (n=30, 54.5%) and 'Middle-Old' (n=25, 45.5%).

Of the male patients, 82.8% (n=24) showed eccentric LVH. The prevalence of LVH varied among the mitral severity grades. In the mild-moderate grade, 20.8% (n=5) of patients displayed eccentric LVH, conversely, 20% (n=1) of patients showed CR. In the moderate severity grade, 25% (n=6) had eccentric LVH, and 60% (n=3) had CR. In the moderate-severe and severe grades, eccentric LVH was present in 29.2% (n=7) and 25% (n=6) of patients, respectively. In moderate-severe MR, 20% (n=1) of the patients exhibited CR. None of the cases with CR were observed in severe grades. Of the female patients, 57.7% (n=15) displayed eccentric LVH. Alike males, the prevalence of LVH varied among mitral insufficiency grades. In the mild-moderate grade, 6.7% (n=1) had eccentric LVH, whereas 36.4% (n=4) showed CR. In the moderate MR group, 46.7% (n=7) had eccentric LVH, and 45.5% (n=5) had CR. In the moderate-severe grade, 26.7% (n=4) had eccentric LVH, and 9.1% (n=1) had CR. In the severe grade, 20% (n=3) had eccentric LVH, and 9.1% (n=1) had CR. It is important to note that, eccentric LVH was commonly predominant in both male [eccentric LVH =82.8% (n=24) *vs.* CR =17.2% (n=5), P=0.26] and female patients [eccentric LVH =57.7% (n=15) *vs.* CR =42.3% (n=11), P=0.05]. Besides, CR was observed to be more frequent in females. However, exceptionally with moderate MR, the males had the highest prevalence with CR (n=17, 60%). Conversely, the females had the highest incidence of eccentric LVH (n=12, 46.7%). *Figure 5C* demonstrates the prevalence of LVH between males and females where the LVH prevalence differed significantly within females with mild-moderate MR (P=0.04).

In the 'Young-Middle' age group (n=30), 20 cases demonstrated an eccentric LVH (66.7%), with a higher prevalence detected in moderate and moderate-severe grades (n=8, 40%, and n=8, 40%, respectively). No cases were observed within mild-moderate MR, and 20% (n=4)

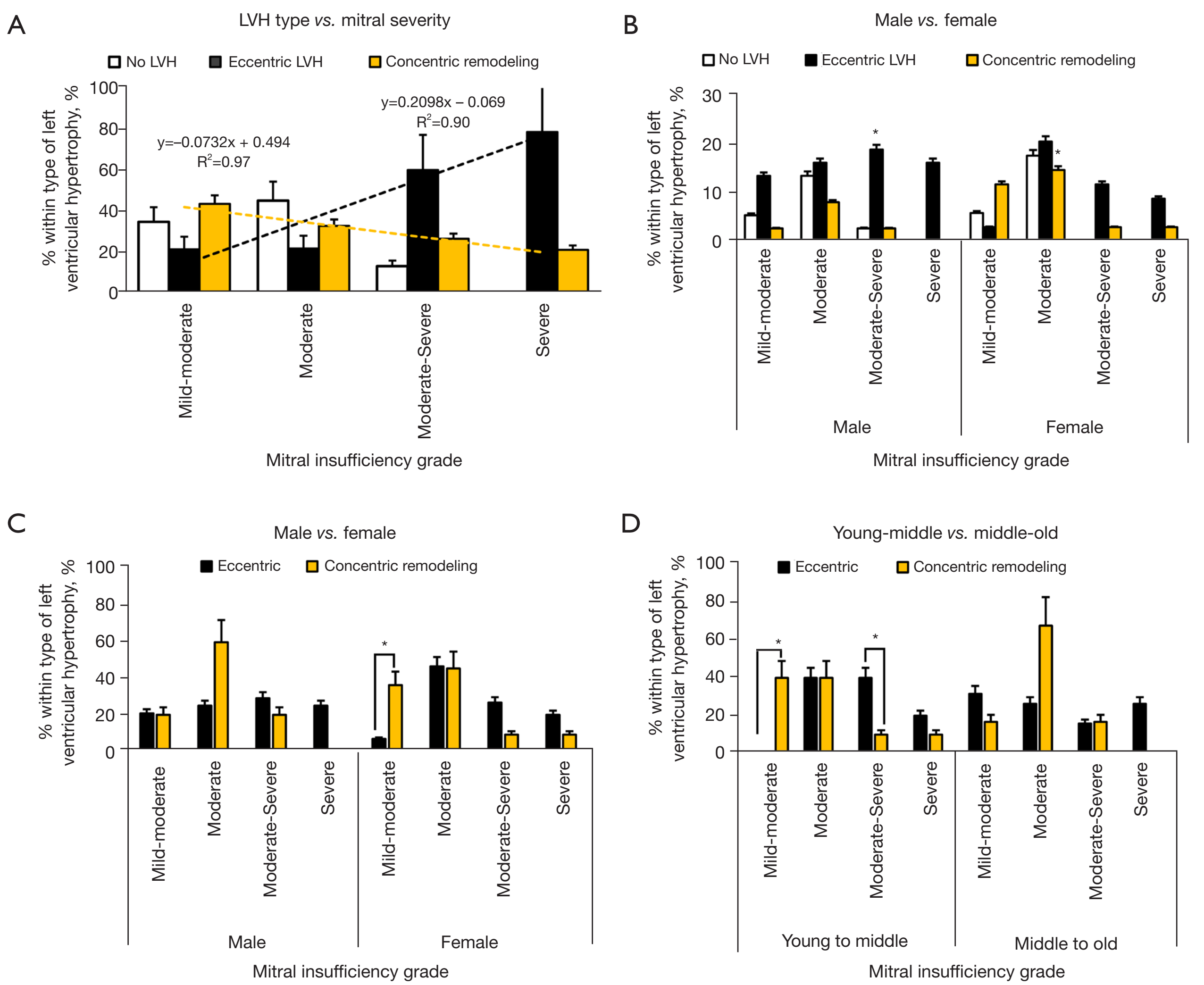

Figure 5 Relationship between LVH types and chronic primary MR severity. (A) Illustrates the relationship between each type of LVH with MR severity. Eccentric LVH shows a high association with increased MR severity and concentric remodeling with decreased MR severity; (B) illustrates the relationship stratified by sex. Eccentric LVH demonstrates a high association among male patients with moderate-severe MR and concentric remodeling among female patients with moderate MR (*, P<0.05); (C) demonstrates the prevalence of LVH with persistent MR among males and females. Notable differences are observed in females with mild-moderate MR (*, P<0.05); (D) shows the prevalence of LVH with persistent MR between two age groups (Group 1: 'Young-Middle' age, Group 2: 'Middle-Old' age). There are no notable differences between age groups, but significant differences are observed within the 'Young-Middle' age groups in LVH types with mild-moderate and moderate-severe MR (*, P<0.05). Non-commercial and no derive reuse with exemptions from licenses of the *Journal of Cardiovascular Magnetic Resonance* under the journal's copyright policy CC BY-NC-ND https://s100.copyright.com/AppDispatchServlet?publisherName=ELS&contentID=S1097664724007476&orderBeanReset=true. Source: Monisha Srabanti, Julio Garcia. Kiosk 6R-TA-11 - Quadratic Stratification of Left Ventricular Hypertrophy and Relationship with Mitral Insufficiency Grading: A Retrospective Study Using Cardiac Magnetic Resonance. *Journal of Cardiovascular Magnetic Resonance*. 2024;26(Supplement 1):100756. LVH, left ventricular hypertrophy; MR, mitral regurgitation.

were observed in severe MR. Conversely, 10 cases (33.3%) displayed CR. The percentages within the type of LVH were 40%, 40%, 10%, and 10% (n=4, 4, 1, 1, respectively) for mild-moderate, moderate, moderate-severe, and severe grades, respectively. In the 'Middle-Old' age group (n=25), 19 individuals showed an eccentric LVH (76%), with the highest prevalence observed in mild-moderate MR (n=6, 31.6%) followed by moderate (n=5, 26.3%), severe (n=5, 26.3%), and moderate-severe (n=3, 15.8%) MR. Additionally, six cases showed CR (24%), with unreliable prevalence across all mitral groups. The percentages for CR within the type of LVH were 16.7%, 66.7%, 16.7%, and 0% (n=1, 4, 1, 0, respectively) for mild-moderate, moderate, moderate-severe, and severe insufficiency grades; respectively. These findings indicate a significant prevalence of eccentric LVH, specifically in the 'Young-Middle' age group with moderate-severe MR. Patients in the 'Middle-Old' age group with moderate MR showed the highest prevalence of CR.

For both age and sex-based studies, while there were noticeable differences in the prevalence of LVH type for both sex and age groups, we only found significant differences in LVH prevalence for the 'Young-Middle' age group (P=0.01). The post hoc test revealed a significant difference in LVH prevalence within the mild-moderate severity group and the moderate-severe severity group (P=0.01, P=0.02, respectively). *Figure 5D* demonstrates the prevalence of LVH among age groups.

Effect of an unhealthy lifestyle on developing LVH (stratified by BMI and sex)

Of the 71 cases, some variables had missing data in the self-reported lifestyle status (smoking cigarettes, consumption of alcohol, nicotine, and caffeine). A descriptive statistics analysis was conducted on the dataset, and we determined that the data was missing completely at random (MCAR). Therefore, we chose to handle the missing data through exclusion to prevent potential biases.

Cigarette smoking

Out of the 71 patients, 52 cases were concluded in this analysis, n=10 were smokers (19.2%) and n=42 were non-smokers (80.8%). The risk factors associated with developing eccentric LVH were cigarette smoking and BMI. The odds ratio (OR) for cigarette smoking [OR 1.65, 95% confidence interval (CI): 1.31–6.52], indicated an increased risk of developing eccentric LVH in smokers. The OR for BMI (OR 1.02, 95% CI: 0.56–1.26), suggested a weaker association between BMI and eccentric LVH. BMI groups were the only factor found to be significant in CR. The OR suggested a potential association between CR and sex (OR 5.55, 95% CI: 4.84–37.94) or cigarette smoking (OR 2.36, 95% CI: 2.18–27.47). However, further investigation is warranted due to the wide range in the CI. The OR for BMI (OR 1.84, 95% CI: 1.25–3.91) indicated an increased risk of CR with a higher BMI range. Among the analyzed cases, non-smokers had the highest occurrence of no LVH (n=26, 62.5%) followed by eccentric LVH (n=16, 35%) with moderate MR. Conversely, smokers had the highest incidence of eccentric LVH (n=4, 40%) with moderate MR. Among the different weight categories, individuals with obesity had the highest occurrence of eccentric LVH with moderate MR (n=10, 33.3%). Overweight individuals followed closely with a (n=11, 37.5%) incidence of eccentric LVH with moderate MR. Obese patients had the highest existence of CR with moderate-severe MR (n=11, 50%) and severe MR (n=11, 50%). *Figure 6A* shows the impact of cigarette smoking, BMI, and sex on developing LVH. *Figure 6* and *Figure 7A* show the degree of prevalence through a color scale.

Alcohol consumption

Out of the 71 patients, 53 cases were considered in this analysis. Reported consumptions were 'Never-Rarely' (n=26, 49.1%) in Group 1 and 'Occasionally-Regularly-Frequently' (n=27, 50.9%) in Group 2. The risk factors associated with developing eccentric LVH were alcohol consumption and BMI. The OR for both alcohol consumption (OR 1.15, 95% CI: 0.26–1.34) and BMI (OR 1.13, 95% CI: 0.66–1.59) suggested a potential association with eccentric LVH. On the other hand, alcohol consumption, BMI, and sex were found to be factors influencing CR. On the other hand, the OR for alcohol consumption (OR 1.15, 95% CI: 0.30–1.41), BMI (OR 1.32, 95% CI: 0.86–2.48), and sex (OR 1.35, 95% CI: 1.13–6.94), indicated a potential influence on CR. The highest prevalence of eccentric LVH (n=9, 33.3% and n=10, 37.5%, respectively) was observed among individuals with overweight and obesity, particularly in those who consume alcohol and had moderate-severe MR. Surprisingly, eccentric LVH was also prevalent among non-alcoholic individuals with a normal weight (n=11, 44.4%) but with moderate-severe MR. Additionally, non-alcoholic individuals with overweight also showed a notable prevalence of eccentric LVH (n=15, 60.5%) with moderate-severe MR. Overweight individuals (n=20) who

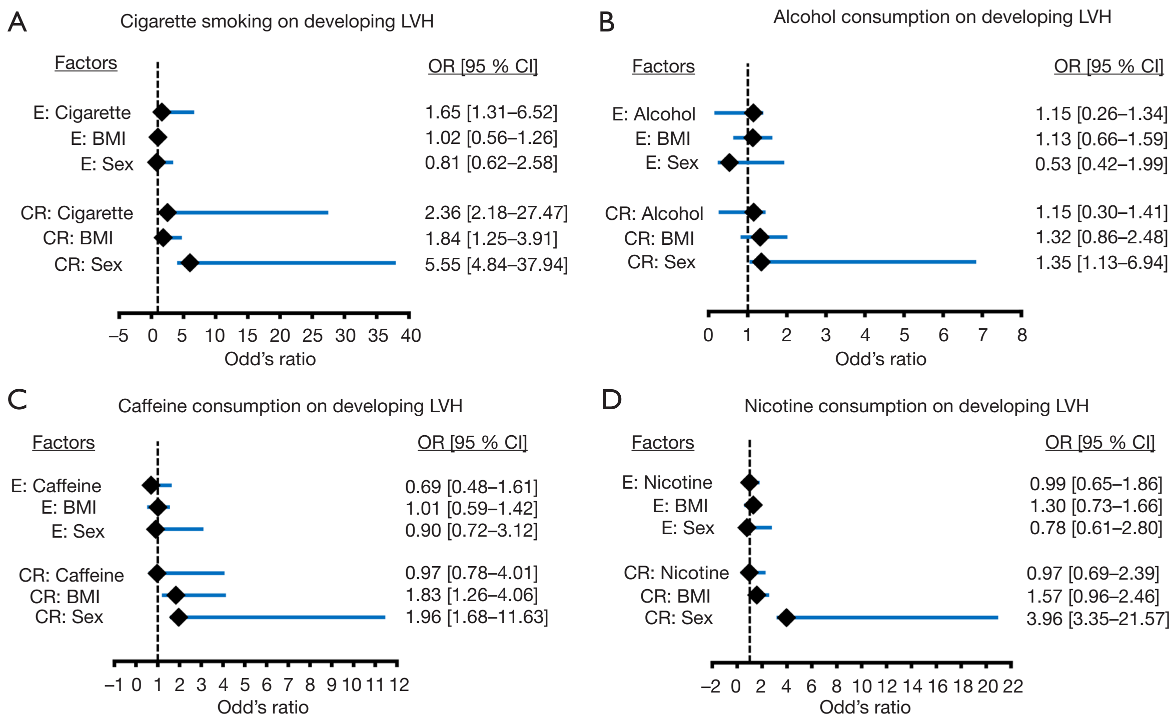

Figure 6 Impact of unhealthy lifestyle choices on developing LVH with persisting MR. The results are shown as OR with 95% CI. (A) Shows the impact of cigarette smoking, BMI, and sex; (B) shows the impact of alcohol consumption, BMI, and sex; (C) reveals the impact of caffeine consumption, BMI, and sex; (D) reveals the impact of nicotine consumption, BMI, and sex. Non-commercial and no derive reuse with exemptions from licenses of the *Journal of Cardiovascular Magnetic Resonance* under the journal's copyright policy CC BY-NC-ND https://s100.copyright.com/AppDispatchServlet?publisherName=ELS&contentID=S1097664724007476&orderBeanReset=true. Source: Monisha Srabanti, Julio Garcia. Kiosk 6R-TA-11 - Quadratic Stratification of Left Ventricular Hypertrophy and Relationship with Mitral Insufficiency Grading: A Retrospective Study Using Cardiac Magnetic Resonance. *Journal of Cardiovascular Magnetic Resonance*. 2024;26(Supplement 1):100756. LVH, left ventricular hypertrophy; OR, odds ratio; CI, confidence interval; BMI, body mass index; E, eccentric; CR, concentric remodeling; MR, mitral regurgitation.

consumed alcohol showed a significant prevalence of CR (n=11, 57.1%) with mild-moderate MR. Non-alcoholic individuals also showed an association with CR (n=9, 42.1%) with moderate MR. *Figure 6B* shows the impact of alcohol consumption, BMI, and sex on developing LVH. *Figure 6* and *Figure 7B* show the degree of prevalence through a color scale.

Caffeine consumption

Among 71 patients, 47 were concluded in this study. The collected caffeine consumption status was 'No or Rarely' (n=12, 25.5%), 'Occasionally or Regularly' (n=30, 63.8%), and 'Frequently or Heavily' (n=5, 10%). Caffeine consumption was not identified as a risk factor for developing either eccentric LVH (OR 0.69, 95% CI: 0.48–1.61) or CR (OR 0.97, 95% CI: 0.78–4.01). However, BMI groups were potentially associated with both eccentric LVH (OR 1.01, 95% CI: 0.59–1.42) and CR (OR 1.83, 95% CI: 1.26–4.06). Sex was only found to be related to CR (OR 1.96, 95% CI: 1.68–11.63), although the result was uncertain due to a wide range in the CI. Overweight individuals had the highest occurrence of eccentric LVH with moderate MR (n=6, 44.4%), while the people with obesity and normal weight had a frequency of no LVH with moderate MR (n=5, 80%) and mild-moderate MR (n=3, 50%), respectively. *Figure 6C* demonstrates the impact of caffeine consumption, BMI, and sex on developing LVH. *Figure 6* and *Figure 7C* show the degree of prevalence through a color scale.

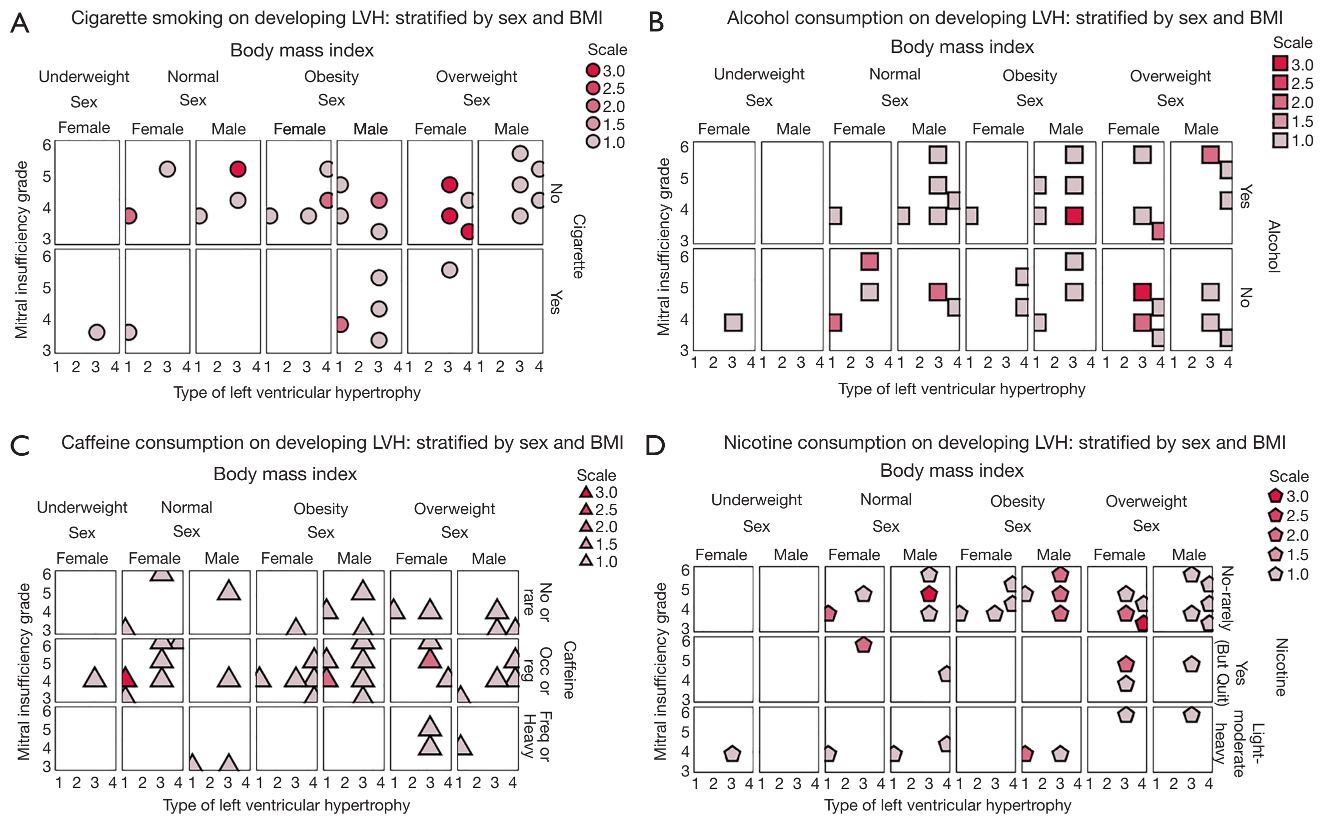

Figure 7 Impact of unhealthy lifestyle choices based on prevalences, stratified by sex and BMI groups (underweight, normal weight, obesity, and overweight). The results show LVH prevalence with an ascending scale from 1 to 3. (A) Illustrates the impact of cigarette smoking; (B) shows the impact of alcohol consumption; (C) reveals the impact of caffeine consumption; (D) reveals the impact of nicotine consumption. Mitral insufficiency grade: 3 = mild-moderate; 4 = moderate; 5 = moderate-severe; 6 = severe. Type of LVH: 1 = no LVH; 2 = concentric LVH; 3 = eccentric LVH; 4 = concentric remodeling. LVH, left ventricular hypertrophy; BMI, body mass index; Occ, occasionally; Reg, regularly; Freq, frequently.

Nicotine consumption

Out of 71 patients, 53 were included in this analysis. Among them, n=36 (66.9%) reported 'No or Rare' nicotine consumption, n=10 (18.9%) reported 'Light-Moderate-Heavy' consumption, and n=7 (13.2%) reported that they previously consumed nicotine but had quit ('Yes but Quit'). The OR indicated no impact of nicotine consumption on developing either LVH subtype (OR 0.99, 95% CI: 0.65–1.86 for eccentric LVH and OR 0.97, 95% CI: 0.69–2.39 for CR). However, BMI groups were associated with both eccentric (OR 1.30, 95% CI: 0.73–1.66) and CR (OR 1.57, 95% CI: 0.96–2.46). The OR suggested a potential association between sex and CR, but further investigation is warranted due to a wide range in the CI (OR 3.96, 95% CI: 3.35–21.57). Eccentric LVH was prevalent among obese people with moderate MR (n=5, 45.5%) and overweight people with moderate-severe MR (n=4, 33.33%) who rarely consume nicotine. CR was prevalent in overweight (n=4, 57.1%, mild-moderate MR). *Figure 6D* shows the impact of nicotine consumption, BMI, and sex on developing LVH. *Figure 6* and *Figure 7D* show the degree of prevalence through a color scale.

Discussion

Our main findings derived from MRI assessment demonstrated that: (I) classification of LVH using CMR parameters was a feasible approach; (II) eccentric LVH had a significant association with increased severity and concentric LVH had a significant association with decreased insufficiency grading of chronic primary MR; (III) significant sex-based association was observed among female patients exhibiting moderate MR with CR. Male patients exhibiting moderate-severe MR with eccentric LVH; (IV) there was no significant association observed between the type of LVH and MR severity grading stratified by age groups ('Young-Middle' and 'Middle-Old'); (V) the eccentric LVH was significantly prevalent in the 'Young-Middle' age group. The LVH prevalence differed significantly among the patients with mild-moderate and moderate-severe MR; (VI) eccentric LVH was commonly prevalent in both male and female patients. In moderate MR, males had a higher prevalence of CR compared to females; (VII) cigarette smoking and alcohol consumption in combination with increased BMI was associated with the development of eccentric LVH; (VIII) CR was primarily influenced by BMI; (IX) caffeine and nicotine consumption did not appear to be risk factors of LVH.

MR is a powerful risk factor for LVH. Szymczyk *et al.* revealed that significantly advanced grades of MR were associated with progressive enlargement of LV which leads to LVH (11). CMR is an effective method for determining the presence of LVH. It provides accurate and consistent measurements of LV mass and LVH pattern (28). A study by Zia *et al.* suggested that mitral valve prolapse (MVP) was associated with concentric basal hypertrophy of the LV. They also showed that the severity of MR (primary MR or type II MR) was related to LVH (29). Our CMR-based study showed that eccentric LVH had the strongest association with a severe form of chronic primary MR with increased LV volume and LV mass, followed by a stronger association with moderate-severe MR, respectively. Conversely, CR had a stronger association with mild-moderate MR and showed a decreasing trend with MR severity.

A CMR-based study by Miller *et al.* showed that sex-specific factors influence LV remodeling in cardiac patients where men were more prevalent (28). However, they did not define which LVH type differed most by sex. Another prior CMR-based study by Tower-Rader *et al.* revealed significant sex differences in LV remodeling in patients with chronic aortic regurgitation (AR), particularly in women. Their study lacked the differentiation of LVH type and could not conclude the relationship with the specific type of LVH (30). Our study observed a significant association between each type of LVH and MR severity among males and females. The association was driven by a higher proportion of males with eccentric LVH who had moderate-severe MR compared to females. On the contrary, a higher proportion of females with moderate MR showed an association with CR.

The aging and elderly population has a higher risk of developing cardiovascular disease (31). Previous studies showed that increased age is associated with LV remodeling marked by an increased mass-to-volume (M/V) ratio as well as with an increase in RWT (31-33). A study by Cheng *et al.* showed that biological aging likely contributes to alterations in LV remodeling, and they have used CMR for assessment. They used two age groups for their study to demonstrate their result and reported that young individuals were more likely to develop LV remodeling than an older individual (32). However, again it was unclear which type of LVH was associated with young individuals. Earlier investigations were done using Echo methods including M-mode Echo for estimating LV mass. Echo has less ability than cardiac MRI to distinguish between CR and eccentric LVH (34). Therefore, our study utilized CMR due to its advantages over Echo. A prior MRI-based study by Alfakih *et al.* reported reduced LV mass in older adults compared to younger adults in a smaller population (35). Another study carried out by Gidding mentioned that younger adults with obesity and hypertension are associated with LVH. They also mentioned that MRI is a better approach than Echo in quantifying LVM which is the key marker for LVH evaluation (36). Our study aimed to find the association between each type of LVH and mitral severity stratified by two age groups (below 60 years = 'Young-Middle' and above 60 years = 'Middle-Old'). As stated in previous studies, reduced LV was more prevalent among the older population, leading us to our 1st and 2nd targets for this aim (32,35). Firstly, we aimed to find an association between the 'Middle-Old' age group and CR with progressive MR. Secondly, we aimed to find an association between the 'Young-Middle' age group and eccentric LVH with progressive MR. However, no significant association was observed between the age groups, LVH, and MR severity. Our sample size was 71, with two age groups. In our study, there were no cases with a young male, which led us toward an insignificant association. A further investigation is warranted with a proper distribution of samples between age groups. Besides, more age groups shall be considered to find a precise association with types of LVH and MR severity.

Cuspidi *et al.* carried out a study on the prevalence of LVH, assessed by echocardiography. They showed the prevalence of eccentric LVH was higher than concentric LVH in hypertensive patients. They also reported that LVH prevalence was not different between women and men in cases with hypertension (6). Another study by Kontos *et al.*

reported that LVH was positively associated with moderate MR in women. They also reported that the prevalence of eccentric LVH was higher in moderate MR compared to hypertensive cases (37). Our study demonstrated the overall prevalence of eccentric LVH being more frequent than CR in patients with chronic primary MR. We also found a higher prevalence of eccentric LVH in men than women and vice versa for CR. Interestingly, only in cases of moderate MR, males had the highest prevalence of CR (60%), while females had the highest incidence of eccentric LVH (46.7%) compared to other types of LVH. Similar results were found in hypertensive cases, as reported by Kontos *et al.* Most of the previous studies were based on echocardiography and our study played a vital role in demonstrating the LVH prevalence in mitral patients using CMR. A prior study by Cuspidi *et al.* on the age-related prevalence of severe LVH showed that increasing age was positively associated with concentric LVH. They have demonstrated their result with four age groups (38). Our study revealed that the prevalence of eccentric LVH was higher in patients above 60 years ('Middle-Old') and the prevalence of CR did not differ between the two age groups. Our study revealed a significant difference in LVH prevalence among people under 60 years old ('Young-Middle'). Post hoc tests revealed a significant difference in LVH prevalence within the mild-moderate and moderate-severe MR. Further study with more age groups could lead to a better conclusion for this study.

Certain lifestyle choices, such as smoking cigarettes and consuming alcohol are known to increase the risk of cardiovascular disease. Previous studies have shown that obesity is also a significant factor in the development of LVH (31). Research conducted by Russo *et al.* has found a significant correlation between obesity or being overweight and an increased risk of LV diastolic dysfunction. This was determined through Echo assessment (39). Similarly, Avelar *et al.* utilized an Echo assessment to establish a link between severe obesity and LVH. However, previous studies have not identified which type of LVH is associated with the negative effects of obesity, and none have demonstrated a connection between MR severity levels (40). Therefore, our study filled that gap and used the BMI groups and sex as the stratifying variables to find the impact of unhealthy lifestyles on developing LVH within different severity grades of chronic primary MR. Most of the prior studies just focused on establishing a general relationship between the development of LVH and unhealthy lifestyle by using Echo analysis. That is how it revealed a platform for us to find the relationship using CMR as the imaging modality.

Cigarette smoking

A prior study by Payne *et al.* reported that cigarette smoking and SBP are associated with LV remodeling in young men. They also revealed that smoking had a positive association with changes in LVM (41). A very recent Echo study by Skipina *et al.* showed that passive smoking is equally associated with LV remodeling, and it was more prevalent in obese people (42). A similar study by Kamimura *et al.* showed that cigarette smoking is an important risk factor for LVH (43). A very recent study by Kolkenbeck-Ruh *et al.* revealed that LVH is highly associated with obesity and tobacco use. They also found a 6% prevalence of LVH in children (44). In our study, cigarette smoking was identified as a risk factor for developing eccentric LVH, while the association between BMI and eccentric was slightly weaker but statistically significant. Interestingly we discovered that cigarette smoking was mildly frequent with being underweight in eccentric LVH. Moreover, non-smokers had the highest occurrence of no LVH (62.5%), while smokers had the highest occurrence of eccentric LVH (40%) with moderate MR. A report by Payne *et al.* demonstrated that the prevalence varies significantly by sex (41). However, in our study, we did not find any significant association with sex who smokes cigarettes. This study suggests that smoking and higher BMI increase the risk of eccentric LVH. Higher BMI also leads to CR. Non-smokers have a lower chance of developing LVH. Overweight individuals are more likely to display certain LVH patterns with MR severity.

Alcohol consumption

A study by Manolio *et al.* showed that alcohol intake was more positively associated with LVH in men than women. However, again it is unclear which type of LVH was associated with it (45). Another study by Li *et al.* concluded that moderate to heavy alcohol consumption was associated with decreased LVEF compared with no-alcohol consumption. It also reveals an association with MR (46). Furthermore, Park *et al.* demonstrated that heavy alcohol users were highly associated with LV chamber remodeling and increased RWT in the Korean population (47). Our study found that alcohol consumption, BMI, and sex play a role in the development of both eccentric LVH and CR in Canadian patients with persisting MR. Individuals with overweight and obesity, especially those who consume alcohol regularly to frequently, appear to be at higher risk for developing eccentric LVH (33.3% and 37.5%, respectively). Non-alcoholic individuals with normal weight (44.4%) and overweight (60.5%) also showed a notable prevalence of eccentric LVH due to moderate-severe MR which is a similar result reported by Li *et al.* (46). Our study showed that CR is more prevalent among females. Besides, overweight individuals who consume alcohol regularly to frequently have a significant prevalence of CR (57.1%) with mild-moderate MR.

Caffeine consumption

Caffeine is a widespread beverage and many studies have been conducted to observe the effect of caffeine consumption on cardiovascular disease. A cross-sectional study by Senftinger *et al.* showed that there was no correlation between the different levels of coffee consumption and cardiovascular diseases, including prior MI and HF. The investigation was done by using electrocardiographic and Echo parameters. Their study demonstrated a correlation between high coffee consumption, raised low-density lipoprotein (LDL) cholesterol levels, and lower SBP-DBP. However, HF was not associated with coffee consumption (48). Similarly, in our study, caffeine consumption was not associated with any subtype of LVH. Additionally, we investigated the association between caffeine consumption and LDL cholesterol (β=0.024, t=0.157, P=0.88), SBP (β=0.136, t=0.585, P=0.56), and DBP (β=−0.284, t=−1.239, P=0.22) in patients with chronic primary MR. We did not find any significant correlation between them. A CMR-based study by Higgins *et al.* found that consuming energy drinks with taurine led to a significant increase in peak systolic strain rate. However, no similar effect was observed with caffeine consumption (49). Our study suggests that caffeine consumption does not appear to be a significant risk factor for the development of eccentric, or CR. Therefore, caffeine intake may not play a substantial role in the pathogenesis of LVH.

Nicotine consumption

Cigarettes and other tobacco products contain nicotine, which is an addictive chemical. Nowadays, cigarette consumption is declining, and the most popular form of nicotine consumption is via electronic cigarettes (e-cig). The impact of cigarettes is known to us however we are still unaware of the effect of e-cig or nicotine on cardiac health, especially in patients with chronic primary MR. The use of nicotine has been linked to hypertension and can potentially activate the renin-angiotensin system when inhaled. This system is responsible for regulating blood pressure (BP). Besides, angiotensin-II (Ang-II), has been shown to contribute to the development of cardiac hypertrophy and fibrosis. An Echo study by Fried *et al.* demonstrated that Ang-II induced the thickening of the LV posterior wall, reducing RWT, and increasing LV mass in nicotine-exposed mice (50). Another similar study by Park *et al.* using echocardiography showed that nicotine consumption is a key factor of LV wall thickening in mice. The LV wall thickening is a key biomarker for diagnosing LVH (51). Knowing that increased LVM is associated with both eccentric and concentric LVH, our study shows no considerable connection between the intake of nicotine and the emergence of any type of LVH. We observed that eccentric LVH was prevalent among obese individuals (45.5%) with moderate MR followed by overweight people (33.33%) with moderate-severe MR who rarely consume nicotine. Conversely, CR was prevalent in overweight people (57.1%, mild-moderate MR) and females (45.5%, moderate MR). According to this analysis, there is no considerable connection between the intake of nicotine and the emergence of LVH. However, BMI was linked to both eccentric LVH and CR. Furthermore, it seems that biological sex might have a probable association with CR, though it is uncertain.

Excessive cigarette and alcohol intake should be considered in chronic primary MR patients with the potential development of LVH. Particularly, in obese people with eccentric LVH. Regardless of the choice of lifestyle, increased BMI and the severity of MR influenced the development of LVH. Therefore, BMI and MR severity grading shall be considered as potential key factors for LVH. On the other hand, caffeine and nicotine consumption do not have any effect on developing LVH in chronic primary MR patients. These results highlight the importance of lifestyle choices and controlling weight in the pathogenesis of LVH.

Limitations and future directions

Several limitations shall be addressed in this study. Firstly, the small cohort size of 71 cases. Secondly, among the 71 cases, there were no cases classified as concentric LVH. Therefore, this study could only establish the relationship between no LVH, eccentric LVH, and CR with the severities of chronic primary MR. Further investigation is needed to reveal the association between concentric LVH and MR severity. Thirdly, while finding the prevalence of LVH type, the cases with no LVH were excluded, leading us towards a smaller population size of 55. Due to the population reduction, the statistical power was low. Additionally, all the lifestyle-related statuses such as smoking cigarettes, and consuming alcohol, caffeine, and nicotine were self-reported. Therefore, the data could be prejudiced. On the other hand, there were missing cases of lifestyle-related status, leading to a further reduction in population size due to exclusion. Many patients hesitate to report their unhealthy lifestyle practices. Thus, alternative approaches shall be considered such as a carbon monoxide (CO) breath test for cigarette smoking, the presence of metabolites in patients' blood systems to identify nicotine consumption, and lab tests such as blood or urine tests for detecting alcohol consumption. In the age groups, there were no cases for young male patients. That is why the groups were considered as over 60 years and under 60 years old to achieve statistical power. A further investigation with more age groups is recommended with an equal distribution of male and female patients for a better conclusion on the association between LVH and MR severity. This study only focused on chronic primary MR and the relationship was demonstrated between severity grading and the types of LVH. A further broader analysis with a larger population is advised on other types of MR such as Functional MR and Carpentier types (I, II, IIIa, and IIIb) to draw a precise conclusion.

Conclusions

This study demonstrates the feasibility of using CMR for LVH and chronic primary MR severity classification in routine practice. This study exhibits that eccentric LVH is highly associated with moderate to severe MR in men under 60 years. In contrast, women with moderate MR are significantly associated with CR. The combination of cigarette smoking and alcohol consumption, along with a higher BMI, increases the risk of developing LVH. Being overweight and obese are strongly linked to eccentric LVH, regardless of an individual's lifestyle choices. On the other hand, consuming nicotine and caffeine does not contribute to the development of any form of LVH. These findings have positive implications for patient risk stratification, follow-up procedures, surgical planning, and MR management.

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Footnote

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Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-466/coif). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Conjoint Health Research Ethics Board at the University of Calgary (REB#13-0902) and informed consent was taken from all the patients.

References

1. Enriquez-Sarano M, Akins CW, Vahanian A. Mitral regurgitation. Lancet 2009;373:1382-94.
2. Fidock B, Barker N, Balasubramanian N, et al. A Systematic Review of 4D-Flow MRI Derived Mitral Regurgitation Quantification Methods. Front Cardiovasc Med 2019;6:103.
3. Feneis JF, Kyubwa E, Atianzar K, et al. 4D flow MRI quantification of mitral and tricuspid regurgitation: Reproducibility and consistency relative to conventional MRI. J Magn Reson Imaging 2018;48:1147-58.
4. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2021;143:e72-e227.
5. Sliwa K, Mocumbi AO. Forgotten cardiovascular diseases in Africa. Clin Res Cardiol 2010;99:65-74.
6. Cuspidi C, Sala C, Negri F, et al. Prevalence of left-ventricular hypertrophy in hypertension: an updated review of echocardiographic studies. J Hum Hypertens 2012;26:343-9.
7. Kawel-Boehm N, Kronmal R, Eng J, et al. Left Ventricular Mass at MRI and Long-term Risk of Cardiovascular Events: The Multi-Ethnic Study of Atherosclerosis (MESA). Radiology 2019;293:107-14.
8. Kagiyama N, Shrestha S. Echocardiographic assessment of mitral regurgitation. J Med Ultrason (2001) 2020;47:59-70.
9. Pype LL, Bertrand PB, Paelinck BP, et al. Left Ventricular Remodeling in Non-syndromic Mitral Valve Prolapse: Volume Overload or Concomitant Cardiomyopathy? Front Cardiovasc Med 2022;9:862044.
10. Gaasch WH, Meyer TE. Left ventricular response to mitral regurgitation: implications for management. Circulation 2008;118:2298-303.
11. Szymczyk E, Wierzbowska-Drabik K, Drozdz J, et al. Mitral valve regurgitation is a powerful factor of left ventricular hypertrophy. Pol Arch Med Wewn 2008;118:478-83.
12. Cesmat AP, Chaudry AM, Gupta S, et al. Left ventricular hypertrophy and ventricular ectopy in mitral valve prolapse. European Heart Journal 2023;44:ehad655.1755.
13. Mann DL. Innate immunity and the failing heart: the cytokine hypothesis revisited. Circ Res 2015;116:1254-68.
14. Tran DT, Silvestri-Elmore A, Sojobi A. Lifestyle Choices and Risk of Developing Cardiovascular Disease in College Students. Int J Exerc Sci 2022;15:808-19.
15. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i-xii, 1-253.
16. Patel MR, White RD, Abbara S, et al. 2013 ACCF/ACR/ASE/ASNC/SCCT/SCMR appropriate utilization of cardiovascular imaging in heart failure: a joint report of the American College of Radiology Appropriateness Criteria Committee and the American College of Cardiology Foundation Appropriate Use Criteria Task Force. J Am Coll Cardiol 2013;61:2207-31.
17. Zange L, Muehlberg F, Blaszczyk E, et al. Quantification in cardiovascular magnetic resonance: agreement of software from three different vendors on assessment of left ventricular function, 2D flow and parametric mapping. J Cardiovasc Magn Reson 2019;21:12.
18. Nayak KS, Nielsen JF, Bernstein MA, et al. Cardiovascular magnetic resonance phase contrast imaging. J Cardiovasc Magn Reson 2015;17:71.
19. Gorecka M, Cole C, Bissell MM, et al. 4D Flow Cardiac MR in Primary Mitral Regurgitation. J Magn Reson Imaging 2024. [Epub ahead of print]. doi: 10.1002/jmri.29284.
20. Apostolakis EE, Baikoussis NG. Methods of estimation of mitral valve regurgitation for the cardiac surgeon. J Cardiothorac Surg 2009;4:34.
21. Schulz-Menger J, Bluemke DA, Bremerich J, et al. Standardized image interpretation and post-processing in cardiovascular magnetic resonance - 2020 update : Society for Cardiovascular Magnetic Resonance (SCMR): Board of Trustees Task Force on Standardized Post-Processing. J Cardiovasc Magn Reson 2020;22:19.

22. Lang RM, Badano LP, Mor-Avi V, 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. J Am Soc Echocardiogr 2015;28:1-39.e14.
23. Gupta AN, Avery R, Soulat G, et al. Direct mitral regurgitation quantification in hypertrophic cardiomyopathy using 4D flow CMR jet tracking: evaluation in comparison to conventional CMR. J Cardiovasc Magn Reson 2021;23:138.
24. Gelfand EV, Hughes S, Hauser TH, et al. Severity of mitral and aortic regurgitation as assessed by cardiovascular magnetic resonance: optimizing correlation with Doppler echocardiography. J Cardiovasc Magn Reson 2006;8:503-7.
25. Khouri MG, Peshock RM, Ayers CR, et al. A 4-tiered classification of left ventricular hypertrophy based on left ventricular geometry: the Dallas heart study. Circ Cardiovasc Imaging 2010;3:164-71.
26. Kawel-Boehm N, Maceira A, Valsangiacomo-Buechel ER, et al. Normal values for cardiovascular magnetic resonance in adults and children. J Cardiovasc Magn Reson 2015;17:29.
27. Gibson PH, Becher H, Choy JB. Classification of left ventricular size: diameter or volume with contrast echocardiography? Open Heart 2014;1:e000147.
28. Miller RJH, Mikami Y, Heydari B, et al. Sex-specific relationships between patterns of ventricular remodelling and clinical outcomes. Eur Heart J Cardiovasc Imaging 2020;21:983-90.
29. Zia M, Valenti V, Cherston C, et al. Severity of mitral valve prolapse is associated with basal left ventricular hypertrophy: a cardiac magnetic resonance study. J Cardiovasc Magn Reson 2012. doi: 10.1186/1532-429X-14-S1-P99.
30. Tower-Rader A, Mathias IS, Obuchowski NA, et al. Sex-based differences in left ventricular remodeling in patients with chronic aortic regurgitation: a multi-modality study. J Cardiovasc Magn Reson 2022;24:12.
31. Levy D. Left ventricular hypertrophy. Epidemiological insights from the Framingham Heart Study. Drugs 1988;35 Suppl 5:1-5.
32. Cheng S, Fernandes VR, Bluemke DA, et al. Age-related left ventricular remodeling and associated risk for cardiovascular outcomes: the Multi-Ethnic Study of Atherosclerosis. Circ Cardiovasc Imaging 2009;2:191-8.
33. Edvardsen T, Detrano R, Rosen BD, et al. Coronary artery atherosclerosis is related to reduced regional left ventricular function in individuals without history of clinical cardiovascular disease: the Multiethnic Study of Atherosclerosis. Arterioscler Thromb Vasc Biol 2006;26:206-11.
34. Alfakih K, Bloomer T, Bainbridge S, et al. A comparison of left ventricular mass between two-dimensional echocardiography, using fundamental and tissue harmonic imaging, and cardiac MRI in patients with hypertension. Eur J Radiol 2004;52:103-9.
35. Alfakih K, Plein S, Thiele H, et al. Normal human left and right ventricular dimensions for MRI as assessed by turbo gradient echo and steady-state free precession imaging sequences. J Magn Reson Imaging 2003;17:323-9.
36. Gidding SS. Controversies in the assessment of left ventricular mass. Hypertension 2010;56:26-8.
37. Kontos J, Papademetriou V, Wachtell K, et al. Impact of valvular regurgitation on left ventricular geometry and function in hypertensive patients with left ventricular hypertrophy: the LIFE study. J Hum Hypertens 2004;18:431-6.
38. Cuspidi C, Meani S, Sala C, et al. Age related prevalence of severe left ventricular hypertrophy in essential hypertension: echocardiographic findings from the ETODH study. Blood Press 2012;21:139-45.
39. Russo C, Jin Z, Homma S, et al. Effect of obesity and overweight on left ventricular diastolic function: a community-based study in an elderly cohort. J Am Coll Cardiol 2011;57:1368-74.
40. Avelar E, Cloward TV, Walker JM, et al. Left ventricular hypertrophy in severe obesity: interactions among blood pressure, nocturnal hypoxemia, and body mass. Hypertension 2007;49:34-9.
41. Payne JR, Eleftheriou KI, James LE, et al. Left ventricular growth response to exercise and cigarette smoking: data from LARGE Heart. Heart 2006;92:1784-8.
42. Skipina TM, Upadhya B, Soliman EZ. Exposure to secondhand smoke is associated with increased left ventricular mass. Tob Induc Dis 2021;19:43.
43. Kamimura D, Cain LR, Mentz RJ, et al. Cigarette Smoking and Incident Heart Failure: Insights From the Jackson Heart Study. Circulation 2018;137:2572-82.
44. Kolkenbeck-Ruh A, Soepnel LM, Crouch SH, et al. Obesity, hypertension, and tobacco use associated with left ventricular remodeling and hypertrophy in South African women: Birth to Twenty Plus Cohort. BMC Cardiovasc Disord 2022;22:403.
45. Manolio TA, Levy D, Garrison RJ, et al. Relation of

alcohol intake to left ventricular mass: The Framingham Study. J Am Coll Cardiol 1991;17:717-21.
46. Li Z, Guo X, Bai Y, et al. The Association Between Alcohol Consumption and Left Ventricular Ejection Fraction: An Observational Study on a General Population. Medicine (Baltimore) 2016;95:e3763.
47. Park SK, Moon K, Ryoo JH, et al. The association between alcohol consumption and left ventricular diastolic function and geometry change in general Korean population. Eur Heart J Cardiovasc Imaging 2018;19:271-8.
48. Senftinger J, Nikorowitsch J, Borof K, et al. Coffee consumption and associations with blood pressure, LDL-cholesterol and echocardiographic measures in the general population. Sci Rep 2023;13:4668.
49. Higgins JP, Yarlagadda S, Yang B. Cardiovascular Complications of Energy Drinks. Beverages 2015;1:104-26.
50. Fried ND, Oakes JM, Whitehead AK, et al. Nicotine and novel tobacco products drive adverse cardiac remodeling and dysfunction in preclinical studies. Front Cardiovasc Med 2022;9:993617.
51. Park SK, Ryoo JH, Kang JG, et al. Smoking Status, Intensity of Smoking, and Their Relation to Left Ventricular Hypertrophy in Working Aged Korean Men. Nicotine Tob Res 2021;23:1176-82.

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