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Association of blood pressure and left ventricular mass with subclinical coronary atherosclerosis

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ABSTRACT

Background Left ventricular (LV) mass is closely associated with atherosclerotic heart disease, but the mechanisms are not well defined. This study aimed to evaluate the risk factors associated with LV mass and subclinical coronary atherosclerosis, in an Asian population free of baseline cardiovascular disease.

Methods The SingHEART study is a population-based cohort in which individuals underwent ambulatory blood pressure (BP) monitoring, cardiac MRI to measure indexed LV mass index (LVMI) and coronary artery calcium (CAC) scoring. Individuals were stratified based on LVMI and the presence of CAC, and intergroup differences in risk factors were analysed. Logistic regression models were used to assess the interaction of BP and LVMI on prevalent CAC.

Results The study included 880 subjects (mean age 45.8±11.7 years, 51.4% women). Individuals with high LVMI had higher BP than those with normal LVMI. Across all LVMI groups, higher BP was associated with the presence of CAC. Compared with individuals with normotensive BP and normal LVMI, those with normotensive BP and high LVMI had no increased risk of prevalent CAC (p=0.530); however, risk was progressively higher in those with hypertensive BP and normal LVMI (risk ratio (RR) 1.47, 95% CI 1.13 to 1.91), or hypertensive BP and high LVMI (RR 1.72, 95% CI 1.26 to 2.36).

Conclusions In this healthy asymptomatic population, hypertension was the strongest risk factor for high LVMI and prevalent CAC. LV hypertrophy was a risk modifier, and its prognostic significance in adults without hypertension requires further study.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Although the prognostic implications of left ventricular (LV) hypertrophy have been well studied, there is the paucity of data on the interaction between hypertension and LV mass in atherosclerotic heart disease, especially in the asymptomatic subclinical phases.

WHAT THIS STUDY ADDS

⇒ The present study in a healthy, asymptomatic Asian population revealed blood pressure (BP) was the strongest risk factor for high LV mass and the presence of coronary artery calcium. LV hypertrophy is a risk modifier that may hold less prognostic significance in healthy individuals without hypertension.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings reinforce the need for tight BP control for primary prevention in healthy populations and highlight the utility of ambulatory BP monitoring for better risk stratification of patients with increased LV mass.

INTRODUCTION

Left ventricular (LV) mass is a predictor of adverse cardiovascular events in individuals with or without known cardiovascular disease.[1 2] Although the prognostic implications of LV hypertrophy have been well studied, there is the paucity of data on the interaction between hypertension and LV mass in atherosclerotic heart disease, especially in the asymptomatic subclinical phases. It is unclear if it is the LV hypertrophy that directly mediates the pathogenesis of coronary atherosclerosis, or if it is the pathogenic drivers of LV hypertrophy, such as hypertension, that promote atherosclerotic disease.[3] This is clinically important when we consider following up LV hypertrophy phenotypes for atherosclerotic disease. We need to understand whether all of them have similar risks for developing atherosclerotic disease, and if there are modifiable risk factors.

Among the modifiable risk factors, blood pressure (BP) has the strongest evidence for a causative relationship with cardiovascular disease.[4] Hypertension not only shares common mechanisms with the pathogenesis of atherosclerosis,[5] but also leads to cardiac remodelling and LV changes.[6] Even in asymptomatic disease, hypertension contributes to coronary artery calcium (CAC),[7] which is a specific marker of coronary atherosclerosis and a robust predictor of cardiovascular outcomes.[8 9]

The present study aimed to evaluate the risk factors associated with LV mass and subclinical coronary atherosclerosis, in a healthy population free of cardiovascular disease at baseline. We examined the hypotheses that BP is the predominant mediator of LV hypertrophy and CAC, and LV mass is a risk modifier influencing coronary atherosclerosis.

MATERIALS AND METHODS

The SingHEART study is a prospective population-based cohort of healthy adults living in Singapore. The study protocol and characteristics, including the full inclusion and exclusion criteria, have been previously described.[10] The present cross-sectional study included the SingHEART cohort at baseline, consisting of male and female volunteers recruited from the general population from October 2015 to October 2019. The inclusion criteria were as follows:

1. Aged 21–69 years old.
2. No known personal medical history of cardiovascular disease (myocardial infarction, coronary artery disease, peripheral arterial disease, stroke).
3. No ongoing use of two or more antihypertensive agents.
4. No known personal medical history of cancer, diabetes mellitus, autoimmune or genetic disease, endocrine disease, psychiatric illness, chronic lung disease or chronic infective disease.

A comprehensive set of investigations was performed at baseline. Standardised questionnaires were used to collect data on demographics, lifestyle and exercise. Basic blood investigations including fasting lipids and glucose, and clinical parameters of height, weight, hip and waist circumference were measured.

Determination of LV mass

Cardiovascular magnetic resonance (CMR) was performed in all participants using either 3T Ingenia (Philips) or 1.5T MAGNETOM Aera (Siemens). Parameters of cardiac mass, volumes and function were measured using the CMR V.42 software (Circle Cardiovascular Imaging) and standardised protocols.[11] LV mass, without papillary muscles, was indexed to body surface area according to the DuBois formula, and LV mass index (LVMI) was used for analysis.[12] Analysis of LVMI was stratified into normal and high, defined as more than one SD away from the mean for each sex. Although CMR reference ranges are well established,[13] they were drawn largely from Western populations, and the normal LV mass is known to be significantly lower in Asians compared with other ethnic groups, even when adjusted for body surface area.[14] Our present study comprises and expands on the cohort in which CMR reference ranges were first described in Singaporean Chinese,[11] hence we adopted cut-offs specific to the distribution within our local cohort. As this is a cohort of the normal population, the number of subjects with LVMI more than 2 SD from the mean was not large enough to perform the analysis, hence the choice of 1 SD instead.

CAC scoring

All subjects aged 30 years and above underwent non-contrast cardiac CT scans using a 320-slice CT scanner. CAC was quantified using Agatston units[15] via Vitrea Workstation, with a score of 0 indicating the absence of any calcified plaque (CAC–), and scores>0 considered positive for coronary atherosclerosis (CAC+).

Physical activity

Participants were issued a Fitbit Charge HR wearable fitness device that was able to track heart rate, step count and intensity of physical activity. The device was worn over a course of 5–7 days. Step counts were retrieved as daily totals, and the mean number of steps in each day was derived. We compiled the mean number of minutes spent daily at various activity intensity levels as defined by Fitbit: sedentary, lightly active (1.5–3 metabolic equivalent tasks (METs)), fairly active (3–6 METs in at least 10 min bouts) and very active (≥6 METs or ≥145 steps per minute in at least 10 min bouts).[16] Active minutes were considered as the sum of lightly active, fairly active and very active minutes.

BP monitoring

BP was assessed via both office and ambulatory pressure monitoring. Office BP and heart rate were measured on the day of volunteer recruitment. Ambulatory BP (ABP) was measured using a cuff monitor (Spacelab Healthcare Model 90227/90217A), as an average over 24 hours, daytime and night-time. BP was then analysed as a continuous variable, as well as categorised into hypertensive or normotensive. Hypertensive BP was defined based on ABP monitoring during the study, regardless of prior diagnosed hypertension or antihypertensive medication use. Diagnostic thresholds followed local and international guidelines[17 18]: 24-hour average BP≥130/80 mm Hg, or daytime average BP≥135/85 mm Hg or night-time average BP≥120/70 mm Hg.

Statistical analysis

Intergroup differences in risk factors were evaluated using χ^2 test for categorical variables and analysis of variance for continuous variables. Subjects in each LVMI group were further subdivided by CAC status (total four subgroups; LVMI/CAC phenotypes), and analysis of variance was used to compare the differences in risk factors across LVMI/CAC phenotypes. The rationale for using categorised variables was to provide feasible cut-offs that can be used in clinical practice. Secondary analysis was performed with a linear regression model, taking LVMI and CAC as continuous variables. Statistical significance was considered as $p<0.05$.

While 39.3% of the study cohort had hypertensive ABP, only 15 (1.7%) individuals self-reported a history of hypertension. Recognising that hypertension is likely under-diagnosed in this population, we assessed the

interaction between hypertensive ABP and LVMI, on the outcome of prevalent coronary atherosclerosis (CAC>0). The study population was grouped as follows:

1. Group 1: normotensive ABP and normal LVMI.
2. Group 2: normotensive ABP and high LVMI
3. Group 3: hypertensive ABP and normal LVMI.
4. Group 4: hypertensive ABP and high LVMI.

Logistic regression models were used to assess risk ratios (RRs) and 95% CI for coronary atherosclerosis among the four groups, with group 1 as the reference group. The model was adjusted for sex, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, creatinine and smoking; it was not adjusted for age or glucose due to limited variability within the cohort. The ABP thresholds most strongly associated with the presence of CAC were determined using the Youden index. Additional analysis was performed using a higher threshold of CAC≥100, which is considered the threshold to consider or initiate statin pharmacotherapy in major global guidelines.[19] Sensitivity analysis was performed, excluding subjects with prior diagnosis of hypertension or who were taking any anti-hypertensive agents.

All statistical analyses were performed using SAS V.9.4.

RESULTS

A total of 880 subjects were included, including 452 (51.4%) women. Clinical characteristics of the study cohort are presented in table 1. The mean age was 45.8±11.7 years, and 91.7% of subjects were of Chinese ethnicity.

Mean LVMI was higher in men (49.8 g/m^2) than women (39.7 g/m^2). High LVMI corresponded to a range of 58.2–91.8 g/m^2 (mean 63.1 g/m^2) in men and 46.7–69.0 g/m^2 (mean 52.6 g/m^2) in women. Individuals with high LVMI, as compared with those with normal LVMI, had higher body mass index, larger waist circumference and higher office and ABP. Men with high LVMI had higher HDL cholesterol and daily calories burned; women with high LVMI had a higher prevalence of smoking.

Factors influencing LVMI/CAC phenotypes

Of the included subjects, 349 men and 396 women underwent CAC scoring. The prevalence of CAC was 28.9%, higher among male (41.8%) than female (17.4%) subjects. Those with high LVMI had significantly higher prevalence of CAC in women (p=0.011), but not in men (p=0.640).

The differences in risk factors across LVMI/CAC phenotypes are presented in online supplemental table S1. BP was significantly higher among those with high LVMI and/or CAC+ in both sexes. ABP over all periods (24 hours, daytime and night-time) was strongly associated with LVMI/CAC (p<0.001).

In women, mean total cholesterol, non-HDL cholesterol, LDL cholesterol and glucose were higher in CAC+ groups. Some wearable-derived physical activity affected LVMI/CAC phenotypes; daily calories burned in men, and sedentary minutes in women.

In the linear regression analyses (online supplemental table S2), there were few significant relationships observed between the risk factors and actual measurement values of LVMI or CAC. Age and ethnicity were the only factors associated with LVMI, while only age was associated with a quantity of CAC.

Effect of hypertension in different LVMI phenotypes on CAC

The prevalence of hypertensive ABP was 39.3% of the entire cohort; prevalence was higher in individuals with high LVMI compared with those with normal LVMI (66.0% vs 39.9%; p<0.001), and in CAC+ individuals compared with those with absent CAC (60.0% vs 36.8%; p<0.001).

Compared with the reference group (normotensive ABP and normal LVMI), there was a significant trend of progressively higher risk of coronary atherosclerosis (CAC>0) across groups 2–4 (p<0.001; table 2, (1) CAC>0), after adjusting for sex, LDL cholesterol, HDL cholesterol, creatinine and smoking. Individuals with normotensive ABP and high LVMI (group 2) had no increased risk for prevalent CAC (RR, 0.83; 95% CI 0.47 to 1.47). However, there was a significantly increased risk for CAC among individuals with hypertensive ABP and normal LVMI (RR, 1.47; 95% CI 1.13 to 1.91); the risk was even greater in those with hypertensive ABP and high LVMI (RR, 1.72; 95% CI 1.26 to 2.36). Adopting a higher threshold, individuals with hypertensive ABP and high LVMI (group 4) had a significantly greater risk of CAC≥100 than the reference group (RR, 3.46; 95% CI 1.20 to 10.87; table 2, CAC≥100). The demographic and clinical profile of groups 1–4 are presented in online supplemental table S3. Sensitivity analyses showed that the interaction effect was consistent after excluding subjects with a prior diagnosis of hypertension (online supplemental table S4).

Thresholds for 24-hour, daytime and night-time ABP that optimally suggest the presence of CAC were 119/80, 121/82, 113/69 mm Hg for men; and 120/76, 123/79, 108/65 mm Hg for women, respectively (online supplemental table S5).

DISCUSSION

This cross-sectional study of 880 healthy individuals in an Asian population found varying influence of sex-specific factors on LVMI and CAC phenotypes. Hypertension is a well-established risk factor for atherosclerosis[5 20] and BP was the consistent risk factor for LVMI and CAC in both sexes. Individuals with high LV mass were at increased risk of CAC>0 only in the presence of hypertensive BP, highlighting an interaction between BP and LV mass in the development of subclinical coronary atherosclerosis.

In our study, in the absence of elevated BP, the presence of high LVMI in healthy adults did not increase the risk of coronary atherosclerosis. In contrast, among

Table 1 Clinical characteristics of study population

	Males				Females			
	Normal LVMI	High LVMI	Overall	P value	Low LVMI	High LVMI	Overall	P value
n	365	63	428		393	59	452	
Age, years	46.0 (12.47)	43.3 (12.05)	45.6 (12.43)	0.104	45.7 (11.20)	47.9 (10.13)	46.0 (11.08)	0.128
Race				**<0.001**				0.642
Chinese	327 (89.6)	54 (85.7)	381 (89.0)		370 (94.1)	56 (94.9)	426 (94.2)	
Indian	20 (5.5)	1 (1.6)	21 (4.9)		9 (2.3)	0	9 (2.0)	
Malay	17 (4.7)	4 (6.3)	21 (4.9)		5 (1.3)	1 (1.7)	6 (1.3)	
Others	1 (0.3)	4 (6.3)	5 (1.2)		9 (2.3)	2 (3.4)	11 (2.4)	
BMI, kg/m^2	24.1 (3.33)	25.6 (3.85)	24.3 (3.45)	0.005	22.8 (3.94)	24.1 (3.78)	23.0 (3.94)	**0.021**
Waist circumference, cm	86.4 (9.76)	89.8 (9.94)	86.9 (9.86)	0.012	78.9 (11.13)	82.1 (10.30)	79.3 (11.07)	**0.031**
Hip circumference, cm	95.9 (8.74)	96.3 (14.0)	96.0 (9.67)	0.865	93.7 (9.72)	95.8 (9.18)	94.0 (9.67)	0.109
24-hour SBP, mm Hg	118.9 (10.47)	126.8 (15.04)	120.1 (11.59)	**<0.001**	110.3 (11.46)	124.7 (16.83)	112.2 (13.20)	**<0.001**
24-hour DBP, mm Hg	75.3 (8.10)	79.4 (11.76)	75.9 (8.85)	**0.009**	69.8 (7.25)	77.8 (9.77)	70.9 (8.08)	**<0.001**
24-hour HR, bpm	71.1 (8.86)	68.7 (8.31)	70.8 (8.82)	**0.035**	72.6 (8.19)	71.7 (8.39)	72.5 (8.21)	0.428
Daytime SBP, mm Hg	121.7 (11.06)	129.3 (15.39)	122.9 (12.08)	**<0.001**	112.7 (11.81)	127.2 (17.32)	114.6 (13.58)	**<0.001**
Daytime DBP, mm Hg	77.5 (8.48)	81.4 (12.04)	78.1 (9.19)	**0.015**	71.8 (7.46)	79.9 (9.83)	72.9 (8.27)	**<0.001**
Daytime HR, bpm	73.9 (8.51)	70.8 (8.56)	73.4 (8.58)	**0.010**	75.3 (8.69)	74.5 (9.13)	75.2 (8.74)	0.537
Night-time SBP, mm Hg	109.5 (14.61)	116.9 (22.03)	110.6 (16.11)	**0.012**	102.9 (15.03)	117.5 (18.43)	104.8 (16.26)	**<0.001**
Night-time DBP, mm Hg	68.2 (10.38)	72.3 (15.55)	68.8 (11.36)	**0.046**	63.7 (10.0)	71.9 (11.45)	64.8 (10.60)	**<0.001**
Night-time HR, bpm	63.0 (10.01)	61.3 (12.08)	62.8 (10.34)	0.274	64.8 (10.11)	63.9 (8.16)	64.7 (9.87)	0.449
Office SBP, mm Hg	130.4 (15.06)	136.3 (13.03)	131.3 (14.92)	**0.002**	120.9 (16.33)	132.9 (19.70)	122.5 (17.26)	**<0.001**
Office DBP, mm Hg	81.2 (10.32)	87.1 (12.76)	82.1 (10.89)	**<0.001**	72.2 (11.91)	80.2 (14.74)	73.2 (12.59)	**<0.001**
Hypertensive ABP	177 (48.6)	40 (63.5)	217 (50.8)	**0.029**	94 (24.1)	35 (59.3)	129 (28.7)	**<0.001**
Prior diagnosed hypertension	4 (0.94)	2 (0.47)	6 (1.41)	**0.196**	3 (0.77)	6 (10.17)	9 (2.00)	**<0.001**
Total cholesterol, mmol/L	5.3 (0.93)	5.4 (1.05)	5.3 (0.95)	0.4534	5.3 (0.94)	5.3 (0.93)	5.3 (0.94)	0.956
HDL cholesterol, mmol/L	1.4 (0.29)	1.5 (0.35)	1.4 (0.30)	**0.0228**	1.6 (0.33)	1.6 (0.29)	1.6 (0.33)	0.976
Non-HDL cholesterol, mmol/L	4.0 (0.91)	4.0 (1.02)	4.0 (0.92)	0.9839	3.7 (0.86)	3.8 (0.88)	3.7 (0.86)	0.945

Continued

Table 1 Continued

	Males				Females			
	Normal LVMI	High LVMI	Overall	P value	Low LVMI	High LVMI	Overall	P value
LDL cholesterol, mmol/L	3.4 (0.82)	3.4 (0.96)	3.4 (0.84)	0.6991	3.3 (0.82)	3.3 (0.76)	3.3 (0.81)	0.891
Triglycerides, mmol/L	1.3 (0.75)	1.2 (0.60)	1.3 (0.73)	0.1988	1.0 (0.55)	1.0 (0.56)	1.0 (0.55)	0.437
Creatinine, µmol/L	81.8 (11.00)	84.0 (11.79)	82.1 (11.14)	0.1719	57.0 (8.48)	56.3 (8.63)	57.0 (8.49)	0.549
Glucose, mmol/L	5.3 (0.67)	5.3 (0.54)	5.3 (0.66)	0.6346	5.1 (0.64)	5.2 (0.51)	5.1 (0.62)	0.394
Smoking	49 (13.5)	10 (15.9)	59 (13.8)	0.615	11 (2.8)	5 (8.5)	16 (3.5)	**0.028**
Alcohol use	105 (28.8)	21 (33.3)	126 (29.4)	0.463	67 (17.0)	14 (23.7)	81 (17.9)	0.212
Daily steps	9185.4 (3309.57)	9737.0 (3823.05)	9267 (3391.01)	0.285	8939.3 (3370.60)	9762.3 (3399.80)	9047 (3382.04)	0.087
Daily distance covered, km	6.7 (2.49)	7.1 (2.76)	6.7 (2.53)	0.283	6.0 (2.29)	6.5 (2.29)	6.0 (2.30)	0.088
Daily minutes sedentary	892.0 (201.53)	917.6 (215.50)	895.7 (203.59)	0.381	876.5 (208.64)	896.3 (249.62)	879.1 (214.23)	0.564
Daily minutes lightly active	186.4 (73.54)	174.3 (076.83)	184.6 (74.07)	0.249	207.3 (79.88)	210.3 (98.11)	207.7 (82.37)	0.823
Daily minutes fairly active	19.9 (17.88)	22.8 (24.52)	20.4 (19.00)	0.384	15.2 (17.66)	17.6 (19.24)	15.5 (17.87)	0.366
Daily minutes very active	22.5 (20.99)	27.3 (25.21)	23.2 (21.70)	0.162	13.8 (15.65)	15.6 (16.63)	14.0 (15.77)	0.434
Daily activity calories	1014.9 (432.68)	1062.2 (521.18)	1022 (446.48)	0.499	729.3 (347.15)	772.1 (393.81)	734.9 (353.43)	0.432
Daily calories burned	2448.4 (387.64)	2587.1 (482.11)	2469 (405.34)	**0.033**	1788.2 (337.11)	1851.5 (303.94)	1796 (333.33)	0.145
CAC done	300	49	349		342	54	396	
CAC>0	127 (42.3)	19 (38.8)	146 (41.8)	0.640	53 (15.5)	16 (29.6)	69 (17.4)	**0.011**

Values are mean (SD) or n (%). Intergroup differences were compared using the χ^2 test for categorical variables and analysis of variance for continuous variables.
Bold values signify significant p-values <0.05

ABP, ambulatory blood pressure; BMI, body mass index; CAC, coronary artery calcium; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HR, heart rate; LDL, low-density lipoprotein; LVMI, left ventricular mass index; SBP, systolic blood pressure.

Table 2 Interaction effect of hypertensive ABP and LVMI on (1) CAC>0 and (2) CAC≥100

	CAC>0				CAC≥100			
	Adjusted*		Unadjusted		Adjusted*		Unadjusted	
Risk groups	RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value
Group 1 (reference): normotensive ABP and normal LVMI								
Group 2: normotensive ABP and high LVMI	0.83 (0.47, 1.47)	0.53	1.12 (0.53, 2.35)	0.774	1.08 (0.11, 10.22)	0.948	0.53 (0.07, 4.08)	0.543
Group 3: hypertensive ABP and normal LVMI	1.47 (1.13, 1.91)	**0.004**	1.91 (1.46, 2.51)	**<0.0001**	2.18 (1.00, 4.79)	0.051	2.69 (1.48, 4.90)	**0.001**
Group 4: hypertensive ABP and high LVMI	1.72 (1.26, 2.36)	**<0.001**	2.73 (2.02, 3.69)	**<0.0001**	3.46 (1.20, 10.87)	**0.034**	4.70 (2.30, 9.62)	**<0.0001**

*Model is adjusted for sex, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, creatinine, smoking.
ABP, ambulatory blood pressure; CAC, coronary artery calcium; LVMI, left ventricular mass index; RR, risk ratio.

individuals with hypertensive ABP, high LVMI significantly accentuated the risk of prevalent subclinical coronary atherosclerosis (CAC>0) and was also associated with more than three times risk of CAC≥100, compared with those with normal LVMI. Previous studies have described an association between LV mass and CAC.[21] The Dallas Heart Study demonstrated that concentric LV hypertrophy was associated with the burden of coronary atherosclerosis relating to quantity of CAC, but not the presence of CAC, independent of confounders including systolic BP or hypertensive status; however, the study did not have ABP measurements.[22] Similarly, another study reported that the presence of concentric LV hypertrophy indicated the presence of CAC, but hypertension status was not an independent factor[23]; however, the study included only patients with suspected coronary artery disease, limiting the generalisability of these findings. Our present study extends the previous evidence by using ABP to evaluate the role of hypertension in the observed relationship between LV mass and CAC in an asymptomatic healthy population. Our findings suggest that BP underpins the association of LV mass and CAC, and LV hypertrophy is a risk modifier that may hold less prognostic significance in healthy individuals without hypertension. It also highlights the importance of conducting ABP tests for patients who have increased LVMI, for better risk stratification and early initiation of treatment for atherosclerotic cardiovascular disease prevention.

Furthermore, our study detected a large number of individuals with hypertensive ABP (39.3%), but only 1.7% reported a prior history of hypertension. The availability of ABP data allows for objective diagnosis of hypertension in our cohort, instead of relying on self-reporting or in-office BP, which is only one of many diagnosis metrics. These findings reflect the limitations of office BP in diagnosis and prognostication of hypertension,[24] and highlight the under-diagnosis of hypertension, which may represent missed opportunities for primary prevention in healthy asymptomatic populations.

Higher BP was also associated with higher LVMI, aligning with previous studies.[25 26] The end-organ damage from hypertension, including LV hypertrophy, has been previously found to be more closely related to ambulatory than office BP, with daytime, night-time and 24-hour BP showing similarly strong correlation.[27] It was not within the purposes of this study to compare the association of ambulatory and office BP to LV hypertrophy; nonetheless, we demonstrate that higher daytime and night-time BP are both correlated with high LVMI. These findings emphasise that night-time BP level is a strong risk factor for LV hypertrophy development,[28 29] underscoring the need for tight night-time BP control. In our supplementary analysis, we looked at optimal BP cut-offs associated with the presence of CAC and found that systolic BP of <120 mm Hg was protective. This is congruent with the findings of the SPRINT trial,[30] and our study articulates increased CAC presence, which is a precursor to future

cardiovascular events, in adults with systolic BP>120 mm Hg.

Lipid levels demonstrated sex-specific differences as risk factors for LVMI or CAC. The presence of CAC was associated with lower HDL cholesterol levels in men, and higher levels of total, non-HDL and LDL cholesterol in women. In risk stratification of asymptomatic individuals, non-HDL cholesterol is most strongly associated with subclinical atherosclerosis compared with other conventional lipid measures[31]; this may account for the reason HDL cholesterol was a significant protective factor for men.

Our study found no association between wearable-derived physical activity and LVMI or CAC. There has been a paradoxical relationship suggested between physical activity and CAC: exercise was linked to increased coronary atherosclerosis in athletes, especially in the most active ones[32]; even in the general population, a large prospective cohort study found a positive correlation between physical activity and the prevalence and progression of CAC.[33] Additionally, wearable data is known to be discrepant with gold standard physical activity measures[34] and this may confound the findings in our study. Our findings do not discredit the indisputable health benefits of physical activity[35]; rather, it highlights the need to create a reliable metric or scale based on the various data points provided by wearables to measure true physical activity.

This study has some limitations. First, our findings were based on the baseline assessment of the SingHEART prospective cohort, hence associations were limited by the cross-sectional nature of this present study. Future follow-up studies on this cohort may reveal clearer longitudinal relationships of risk factors, LVMI and CAC with incident cardiovascular events. Second, the accuracy of wearable-derived physical activity data depended on the subjects wearing the device throughout the day for a complete representation of daily activity, and our analysis did not account for the possibility of incomplete data on certain days. At last, an overwhelming majority of subjects were of Chinese ethnicity despite recruitment from the multiethnic population in Singapore. Our findings thus have limited generalisability to other ethnic groups.

In an Asian population free of cardiovascular disease, hypertension was the strongest risk factor for high LV mass and prevalent CAC, highlighting the importance of BP control in primary prevention. LV mass was not independently associated with CAC, and its prognostic implications in healthy adults without hypertension require further study. Subclinical coronary atherosclerosis was prevalent among asymptomatic individuals with normal BP, supporting the role of CAC for risk stratification and consideration of antihypertensive treatment in these individuals. Further prospective studies may better elucidate the relationships among BP, LV mass and cardiovascular outcomes.

Contributors EDWL and WH contributed equally as first authors to the conception and design of the study, writing of the manuscript. SCK was responsible for data curation. RS served as the lead statistician for the analysis of the data. CJN, SYT, CC, JJLY and KKY reviewed and provided critical comments for the manuscript. All authors have read and approved the final manuscript. WH is responsible for the overall content as guarantor.

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Competing interests KKY has received research funding from Amgen, AstraZeneca, Abbott Vascular, Bayer, Boston Scientific, Shockwave Medical, Novartis (all via institution); Consulting fees from Abbott Vascular, Medtronic, Novartis, Peijia Medical; Speaker fees from Shockwave Medical, Abbott Vascular, Boston Scientific, Medtronic, Alvimedica, Biotronik, OrbusNeich, Shockwave Medical, Amgen, Novartis, AstraZeneca, MicroPort, Terumo, Omnicare. KKY is also cofounder and owns equity in Trisail for which OrbusNeich is an investor. All other authors report no relationships that could be construed as a conflict of interest.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by SingHealth Centralized Institutional Review Board (ref: 2015/2601). Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available on reasonable request. The data that support the findings of this study are not publicly available due to personal data protection and ethical reasons, but can be made available from the corresponding author on reasonable request.

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