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ORIGINAL PAPER

Association of cardiovascular disease risk factors with left ventricular mass, biventricular function, and the presence of silent myocardial infarction on cardiac MRI in an asymptomatic population

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Abstract The purposes of this study were to evaluate the relationship between risk factors for cardiovascular disease (CVD) and cardiac mass and function on cardiac magnetic resonance imaging (MRI), and to investigate possible risk factors for silent myocardial infarction (SMI) in an asymptomatic Asian population. We included 647 asymptomatic subjects (485 males, mean age 54.8 ± 6.7 years; 162 females, mean age 55.2 ± 7.6 years) who underwent 1.5-T cardiac MRI during a health checkup. The association between biventricular functional parameters as evaluated on MRI and CVD risk factors was examined using multivariable regression and analysis of variance. The left ventricular mass-to-volume ratios were positively related to body mass index (β = 0.153, $p < 0.001$), systolic (β = 0.165, $p = 0.001$) and diastolic (β = 0.147, $p = 0.002$) blood pressure, triglyceride levels (β = 0.197, $p = 0.006$), and C-reactive protein levels (β = 0.130, $p < 0.001$), and were negatively related to estimated glomerular filtration rates (β = −0.076, $p = 0.025$). No significant relationship was present between ventricular parameters and the presence of SMI after adjusting for confounders. The prevalence (6.9 %, 7/101) of SMI in diabetics was significantly greater than that in non-diabetics patients (0.9 %, 5/546; confidence interval 1.739–12.848; $p < 0.001$). Traditional CVD risk factors are associated with ventricular mass, geometry and function in asymptomatic subjects. Silent MI may not independently influence ventricular mass and function and diabetes mellitus may contribute to the development of SMI.

Keywords Cardiac magnetic resonance imaging · Asymptomatic subjects · Cardiovascular disease risk factor · Silent myocardial infarction · Myocardial scar · Metabolic syndrome · Ventricular function

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Introduction

Cardiac magnetic resonance imaging (MRI) has been widely accepted as the reference standard for assessment of cardiac structure and function [1–7]. Several studies such as the Multi-Ethnic Study of Atherosclerosis (MESA) have used cardiac MRI to assess cardiac function and its

association with various factors including age, sex, ethnicity and known cardiovascular disease (CVD) risk factors [8–12].

Asymptomatic individuals can still exhibit preclinical cardiovascular problems that may adversely affect cardiac function [4, 8, 9]. Metabolic syndrome (MS) and silent myocardial infarction (SMI) are of particular interest. MS is well known as a multiplex risk factor for CVD according to many various previous reports [13]. In a cohort study, SMI, a condition that can be identified on MRI, was associated with CVD [14]. In addition, mortality from SMI has been shown to be similar to that of recognized MI, suggesting that SMI is a serious medical condition [14–16]. Thus, cardiac abnormalities in asymptomatic individuals may contribute to increases in morbidity and mortality.

All previous studies on this topic were performed in a population of mainly white people with or without a small portion of Asian people [14–18]. As CVD is a leading cause of death with a significant public health burden in Korea [19, 20], the need for an equivalent study in an Asian population is evident. Thus, the aim of this study was to assess cardiac mass and function on cardiac MRI in relation to various CVD risk factors in an asymptomatic Korean population. In addition, we also examined potential risk factors associated with SMI.

Materials and methods

Study population

The study sample initially included 704 subjects over 40 years of age who underwent cardiac MRI for a health checkup at the Health Promotion Center of Samsung Medical Center from September 2009 to June 2013. This study was approved by the institutional review board of our hospital; the need for informed consent was waived due to the retrospective nature of this study. To enroll an asymptomatic population, subjects with a history of clinical coronary artery disease (CAD) or cerebrovascular accident (CVA) were excluded. After initial exclusion, there were a total of 647 subjects (485 men, aged 54.8±6.7 years; 162 women, aged 55.2±7.6 years). In this study, 12 subjects were found to have SMI. Because all of the subjects with SMI were male, only male subjects were included in the reference group. A total of 12 subjects with SMI (mean age, 58.7 years; age range, 50–70 years) and 473 subjects (mean age, 54.8 years; age range, 41–85 years) without SMI were included. This recruitment process is presented in Fig. 1.

Baseline examination

Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m^2). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were

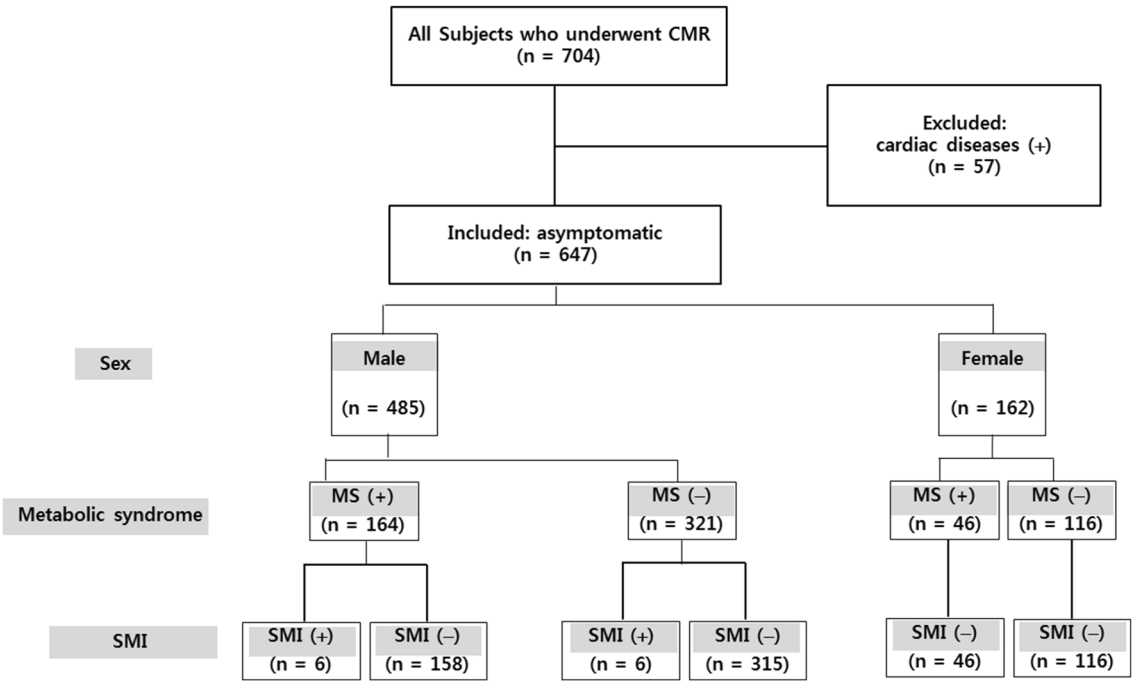

Fig. 1 Flow chart of the study population. *CMR* cardiac MRI, *MS* metabolic syndrome, *SMI* silent myocardial infarction, + presence, – absence. Silent myocardial infarction was present in 7 patients with diabetes mellitus (9.1% of 77 diabetic males and 6.9% of all diabetics)

measured after subjects had rested for at least 5 min. Blood samples were collected from the antecubital vein after overnight fasting. Total cholesterol (TC), high density lipoprotein (HDL), triglyceride (TG), fasting plasma glucose (FPG), and serum creatinine (Cr) levels were measured via enzymatic or colorimetric methods. The estimated glomerular filtration rate (eGFR), which represents kidney function, was calculated using the formula from the Modification of Diet Renal Disease Study: eGFR (mL/min/1.73 m^2) = 186.3 × $(Cr)^{-1.154}$ × $(age)^{-0.203}$ × (0.742 for women) [21]. Information on the presence of hypertension, type 2 diabetes mellitus, smoking and alcohol consumption were obtained from interviews. Body surface area (BSA) was calculated as follows: 0.20247 × height $(m)^{-0.725}$ × weight $(kg)^{-0.425}$.

Definitions

Body weight was classified into three categories according to BMI (normal if BMI <23 kg/m^2, overweight if 23 kg/m^2 ≤ BMI < 25 kg/m^2, obese if BMI ≥25 kg/m^2). Subjects were categorized as having hypertension if they had a SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, a past diagnosis of hypertension, or were taking medication for hypertension. Individuals with a fasting plasma glucose (FPG) ≥126 mg/dL, a past diagnosis of diabetes, or who were on active medication for diabetes were defined as having diabetes. Dyslipidemia was defined as total cholesterol (TC) ≥240 mg/dL, low-density lipoprotein (LDL) cholesterol ≥160 mg/dL, high-density lipoprotein (HDL) cholesterol <40 mg/dL [22], a past diagnosis of dyslipidemia, or if the subject was on active medication for dyslipidemia. Subjects were defined as having CAD if they had a past diagnosis, or if they were on active medication for angina pectoris and/or myocardial infarction. Subjects with a past diagnosis of CVA or who were on active medication for transient ischemic attack, chronic cerebral infarct or stroke were considered to have had a CVA. Chronic kidney disease (CKD) was defined as eGFR < 60 mL/min/1.73 m^2 according to the National Kidney Foundation Kidney Disease Outcome Quality Initiative [21]. MS was defined by the presence of three or more criteria from the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP-III) [23]. We used South Asian-specific values for waist circumference: ≥90 cm in men and ≥80 cm in women. Subjects were considered current smokers if they had smoked within 1 year before the survey date, and as former smokers if they had smoked in their lifetime, but had not smoked for at least 1 year before the survey date. Those who were not current smokers or former smokers were considered nonsmokers.

Acquisition of MRI data

All patients underwent cardiac MRI using a 1.5 T scanner (Magnetom Avanto, Syngo MR B17 version or D13 version with the Tim and Dot System; Siemens Healthcare, Erlangen, Germany) with a 32-channel phased-array receiver coil during repeated breath-holds. After localization, cine images of the left ventricle (LV) were acquired using a steady-state free-precession sequence on 4-chamber, 2-chamber, 3-chamber and short-axis views for obtaining 20–30 contiguous short-axis slices to include the entire LV with a 6-mm slice thickness and 4-mm gaps. In cases of patients with arrhythmias or breathing difficulties, fast cine MRI using the temporal parallel acquisition technique (TPAT; acceleration factor, 3) was used for cine MRI.

Standard delayed gadolinium-enhanced imaging was performed using a phase-sensitive inversion recovery (PSIR) technique 15 min after injection of 0.2 mmol/kg gadobutrol (Gadovist; Bayer Healthcare, Berlin, Germany) using contiguous short-axis image acquisition of 10–12 slices at 6-mm thickness with a 4-mm inter-slice gap. Inversion delay times were typically 280–360 ms.

Cardiac magnetic resonance imaging analysis

Ventricular function was analyzed by an observer with 6 years of experience in cardiac MRI analysis using a commercial software package (ARGUS Workstation; Siemens Healthcare). Short-axial images were used on a per-slice base to measure the volume of both ventricles and the mass of the LV. Standard methods were used for analysis [5, 24]. Papillary muscles and trabeculations were included in the LV and the right ventricle (RV) cavities for volume and mass measurements. In the most basal slice of both ventricles, a rim of myocardium should be visible at more than 50 % of the LV or RV circumference. The contour was drawn to include the LV outflow tract up to the level of the aortic valve cusp. To include the RV outflow tract, the contour was included up to the pulmonary valve.

The ventricular function parameters that were analyzed using MRI data in this study were: end-diastolic wall mass (g), mass index (MI, mass divided by height to the 2.7th power, g/$m^{2.7}$), mass-to-volume ratio (end-diastolic wall mass divided by end-diastolic volume), the end-diastolic volume (EDV, mL), EDV index (EDVI, EDV divided by BSA, mL/m^2), ejection fraction (EF, % by volume), cardiac output (CO, L) and cardiac index [CI (CO divided by BSA), L/m^2] of the LV, and the EDV (mL), EDV index (EDVI, mL/m^2), and EF (% by volume) of the RV. The LV mass-to-volume ratio (M/V), which in the setting of an increased LV mass suggests concentric hypertrophy, was included because it has been reported to be an independent predictor of incident CVD [25, 26]. High signal-intensity foci that were more than 5 mm in size and signal intensity >5 standard deviations from the normal myocardial signal intensity on late gadolinium-enhanced MRI were considered to represent SMI.

Intra-observer and inter-observer variability

Twenty randomly selected subjects were analyzed by two independent observers. Both observers had more than 2 years of experience in cardiac MRI analysis. The EDV and ESV of both ventricles were measured by an observer blinded to the findings of the other observer. The same dataset was evaluated again by each observer 1 month later.

Statistical analysis

Numerical data were expressed as the percentage or mean ± 95 % confidence interval (lower and upper limits). Linear trend testing was performed for the analysis of age-related differences in left and right ventricular function values on cardiac MRI for both sexes. We conducted multivariable linear regression to evaluate the relationship between CVD risk factors and ventricular parameters. We constructed two models: one with MS/SMI status and the other without. In the regression model, demographic factors such as age, sex and body size were included for adjustment. We used height to the 2.7th power instead of body surface area for body size adjustment to avoid underestimating the effect of obesity on cardiac function [27]. When assessing RV function, the corresponding LV parameter was added to the regression model. This additional adjustment was based on the knowledge that LV and RV are interdependent [28]. The risk factors analyzed in multivariable regression included BMI, SBP, DBP, total cholesterol, LDL and HDL cholesterol, TG, FPG, eGFR, C-reactive protein (CRP), smoking status, MS status and SMI status. Smoking status was converted into a trichotomous variable: 2 for current smokers, 1 for former smokers, and 0 for nonsmokers. MS and SMI status were examined as dichotomous variables. For the assessment of the relationship between MS/SMI and cardiac parameters according to sex, analysis of variance (ANOVA) was performed. All statistical analysis was performed using PASW Statistics 18 (IBM, Armonk, NY), and p-values <0.05 were considered statistically significant.

Results

The demographics of the study population are summarized in Table 1. Ventricular parameters according to sex and age are presented in Supplementary Tables 1 and 2.

Mean LVEF and RVEF were higher in females compared with males (68.5 ± 7.2 % versus 66.6 ± 6.2 % for LVEF, $p = 0.004$; and 60.4 ± 8.1 % versus 56.9 ± 7.5 % for RVEF, $p < 0.001$). However, LV mass index, LV M/V, and LVESVI was higher with males (58.2 ± 9.0 g/m^2 versus 46.8 ± 8.1 g/m^2 for LV mass index, $p < 0.001$; 0.82 ± 0.15 versus 0.68 ± 0.13 for LV M/V, $p < 0.001$; 24.3 ± 6.8 mL/m^2 versus 22.5 ± 9.9 mL/m^2 for LVESVI, $p = 0.034$) (supplementary Table 1). Some ventricular function parameters were significantly different among age groups in all sexes in LVEF ($p = 0.001$), LV mass index ($p = 0.042$), LV M/V ($p = 0.001$), RVEF ($p = 0.02$), RVEDV ($p < 0.001$), and RVEDVI ($p < 0.001$). Some ventricular function parameters were different among age groups in males (LVEF, $p = 0.005$; LVEDV, $p = 0.023$; RVEF, $p = 0.009$; RVEDV, $p < 0.001$; RVEDVI, $p = 0.001$) and females (LV mass, $p = 0.034$; LV mass index, $p = 0.009$; LV M/V, $p < 0.001$; RVEDV, $p = 0.001$; RVEDVI, $p = 0.002$) (supplementary Table 2; Fig. 2).

Table 1 Distribution of general characteristics and cardiovascular risk factors in a study population free of coronary artery disease and cerebrovascular accidents (n = 647)

Variables	n (%) or mean ± SD
Age, years, mean ± SD	55.0 ± 7.0
40–49	23.2
50–59	53.3
60–69	20.1
≥70	3.4
Sex, male, %	75.0
Smoking, %	
Non	39.9
Former	34.2
Current	26.0
Alcohol consumption, %	
Current	72.5
Body mass index (g/m^2)	24.5 ± 2.8
Normal, %	28.4
Overweight, %	31.2
Obese, %	40.5
Hypertension, %	39.7
Diabetes mellitus, %	15.6
Dyslipidemia, %	53.2
Chronic kidney disease, %	0.5
Systolic blood pressure, mmHg	120.7 ± 17.2
Diastolic blood pressure, mmHg	77.2 ± 10.4
Total cholesterol, mg/dL	197.4 ± 37.6
Triglyceride, mg/dL	139.2 ± 85.2
LDL cholesterol, mg/dL	125.9 ± 33.2
HDL cholesterol, mg/dL	52.5 ± 13.9
Fasting blood glucose, mg/dL	103.5 ± 22.0
Serum creatinine, mg/dL	0.88 ± 0.16
Estimated glomerular filtration rate, mL/min/1.73 m^2	92.1 ± 15.8
C-reactive protein, mg/L	0.88 ± 0.16
Height, m	1.67 ± 0.08
Body surface area, m^2	1.78 ± 0.16

HDL high density lipoprotein cholesterol, *LDL* low density lipoprotein cholesterol, *SD* standard deviation

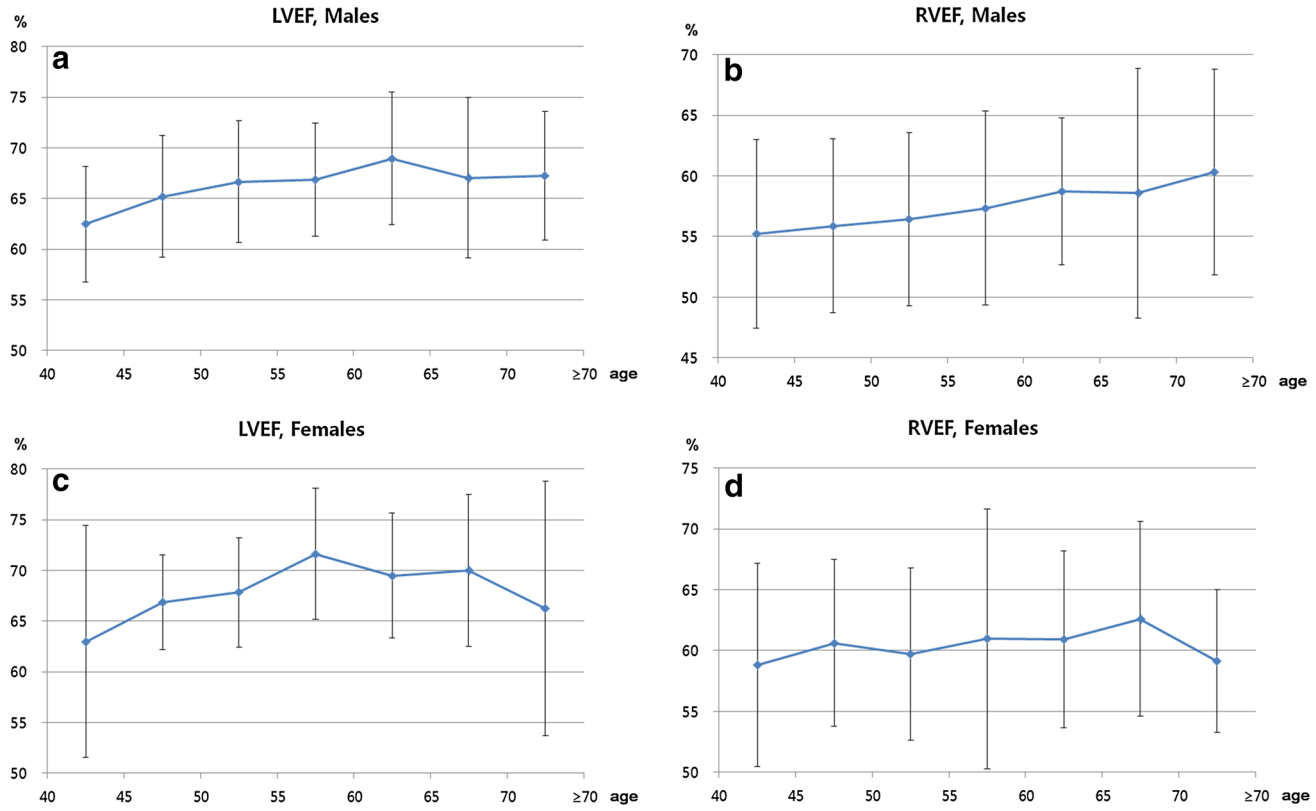

Fig. 2 The influence of aging on biventricular function in both sexes. LVEF and RVEF were different among age groups in males (**a, b**) (LVEF, $p=0.005$; RVEF, $p=0.009$) and not different in females (**c, d**) (LVEF, p = 0.112; RVEF, $p=0.642$). *LVEF* left ventricular ejection fraction, *RVEF* right ventricular ejection fraction

Association between cardiac function and various cardiovascular risk factors

The data obtained from multivariable regression are summarized in Table 2.

Left ventricular parameters:

- LV mass: LV mass was positively associated with BMI (standardized coefficient [β] = 0.322, p < 0.001), SBP (β = 0.251, $p<0.001$), and current smoking (β = 0.129, $p<0.001$). Among the examined ventricular parameters, LV mass was best explained by a multivariable regression model.
- LV mass-to-volume ratio: BMI (β = 0.153, $p<0.001$), SBP (β = 0.165, $p=0.001$), DBP (β = 0.147, $p=0.002$), TG level (β = 0.197, $p=0.006$), and CRP level (β = 0.130, $p<0.001$) were positively associated with LV M/V. eGFR (β = −0.076, $p=0.025$) was negatively associated with LV M/V.
- End-diastolic volume (LVEDV): LVEDV was positively associated with BMI (β = 0.223, $p<0.001$) and SBP (β = 0.153, $p=0.002$). DBP (β = −0.188, $p<0.001$) and TG level (β = −0.204, $p=0.006$) were negatively associated with LVEDV.
- Ejection fraction: LVEF was not associated with any of the CVD risk factors. The adjusted r^2 of the regression model was the smallest among the examined parameters.
- Cardiac output: LVCO was positively associated with BMI (β = 0.279, $p<0.001$), SBP (β = 0.201, $p<0.001$) and FPG level (β = 0.132, $p=0.001$).

Right ventricular parameters:

- End-diastolic volume: RVEDV was positively associated with BMI (β = 0.090, $p<0.001$) and negatively associated with LDL cholesterol (β = −0.225, $p=0.048$), FPG level (β = −0.068, $p=0.004$) and the presence of SMI (β = −0.054, $p=0.016$) when adjusted for demographic variables and the corresponding LV parameter (LVEDV).
- Ejection fraction: RVEF was positively associated with FPG level (β = 0.085, $p=0.029$) and negatively associated with CRP level (β = −0.079, $p=0.027$) when adjusted for demographic variables and the corresponding LV parameter (LVEF).

Table 2 Multivariable analysis of cardiovascular disease risk factors in relation to left and right ventricular parameters in a population free of coronary artery disease and cerebrovascular accidents (n = 647)

	LV parameters					RV parameters	
	Mass	Mass-to-volume ratio	EDV	EF	CO	EDV	EF
Adjusted r^2	0.618	0.359	0.307	0.037	0.251	0.708	0.211
BMI	0.322*	0.153*	0.223*	0.025	0.279*	0.090*	–0.033
SBP	0.251*	0.165*	0.153*	0.093	0.201*	–0.059	0.095
DBP	–0.025	0.147*	–0.188*	–0.073	–0.089	0.002	–0.071
TC	0.092	0.026	0.153	0.443	–0.172	0.226	–0.134
TG	–0.007	0.197*	–0.204*	–0.142	–0.062	–0.094	0.025
LDL	–0.141	–0.036	–0.195	–0.379	0.133	–0.225#	0.106
HDL	–0.025	0.046	–0.084	–0.144	–0.005	–0.085	0.027
eGFR	0.000	–0.076#	0.058	0.003	0.018	0.028	–0.014
FPG	–0.019	0.040	–0.048	0.002	0.132*	–0.068*	0.085#
CRP	0.042	0.130*	–0.052	0.000	0.032	0.002	–0.079#
Smoking status	0.129*	0.071	0.079	–0.074	–0.015	–0.008	–0.027
MS	–0.026	–0.070	0.019	0.022	–0.040	–0.013	–0.014
SMI	0.049	0.060	–0.015	0.023	–0.057	–0.054#	0.068

Data are β coefficients

BMI body mass index, *CO* cardiac output, *CRP* C-reactive protein, *DBP* diastolic blood pressure, *EDV* end-diastolic volume, *EF* ejection fraction, *eGFR* estimated glomerular filtration rate, *FPG* fasting plasma glucose, *HDL* high-density lipoprotein cholesterol, *LDL* low-density lipoprotein cholesterol, *LV* left ventricle, *MS* metabolic syndrome status, *RV* right ventricle, *SBP* systolic blood pressure, *SMI* silent myocardial infarction status, *TC* total cholesterol, *TG* triglyceride

# $p < 0.05$, * $p < 0.01$

Effect of metabolic syndrome on cardiac function

The prevalence of MS in our study population was 32.5% (n = 210). In both sexes, subjects with MS had significantly higher LV mass unadjusted for body size, LV mass adjusted for body size (divided by height$^{2.7}$) and LV M/V (Table 3). In males, subjects with MS had higher LV cardiac output even after adjusting for body size. Ejection fraction was not related to MS status in either sex. None of the volumetric parameters were related to MS status. All of the associations, however, became nonsignificant after adjusting for confounding factors (Table 2).

Assessment of cardiac function in male subjects with silent myocardial infarction and the identification of potential risk factors

The prevalence of SMI in our study population was 1.9% (n = 12, all men) (Fig. 3). Seven of these subjects (6.9%, 7/101) were diabetics. The prevalence of SMI in DM was significantly greater than that in non-DM patients (0.9%, 5/546; confidence interval 1.739–12.848; $p < 0.001$). The prevalence of SMI (2.9%, 6/210) in MS patients was not significantly different compared that in non-MS patients (1.4%, 6/437; confidence interval, –0.923 to 4.889; $p = 0.190$).

Subjects with SMI had a significantly higher LV mass (124.8 ± 23.1 g versus 107.3 ± 19.1 g, $p = 0.002$) and a LV M/V (0.95 ± 0.15 versus 0.82 ± 0.15, $p = 0.002$) (Supplementary Table 3). LV systolic function as measured by ejection fraction was not affected by SMI status (66.2 ± 8.0% versus 66.6 ± 6.2, $p = 0.822$). Those with SMI also had a higher RVEF (61.9 ± 7.4% versus 56.9 ± 7.5%, $p = 0.023$) and lower RVEDV (adjusted for body size)(27.4 ± 5.5 mL/m$^{2.7}$ versus 31.6 ± 6.5 mL/m$^{2.7}$, $p = 0.027$). However, after adjusting for confounders, only RVEDV remained significantly associated with SMI (Table 2).

Intra-observer and inter-observer variability

Interclass coefficients for intra-observer variability were 0.98, 0.99, 0.98, 0.94 and 0.99 for LVESV, LVEDV, LV mass, RVESV and RVEDV, respectively. Interclass coefficients for inter-observer variability were 0.95, 0.88, 0.98, 0.98 and 0.94, respectively.

Discussion

In this study, cardiac mass and function as determined by cardiac MRI were associated not only with traditional CVD risk factors such as high blood pressure, but also with the

Table 3 Comparison of left and right ventricular parameters in subjects with/without metabolic syndrome (n = 647)

	With MS	Without MS	*p*-value
Male (n = 485)	n = 164	n = 321	
Age, years (mean, range)	54.5 (41–74)	55.1 (42–85)	0.304
LV parameters			
EF, %	66.6 ± 6.2	66.6 ± 6.2	0.963
EDV, mL	134.5 ± 23.8	131.8 ± 24.3	0.251
Mass, g	114.2 ± 20.4	104.3 ± 18.0	<0.001
Mass-to-volume ratio	0.86 ± 0.15	0.80 ± 0.15	<0.001
CO, L/min	5.73 ± 0.99	5.46 ± 0.99	0.005
EDV adjusted for height$^{2.7}$, mL/m$^{2.7}$	31.7 ± 5.2	31.3 ± 5.6	0.418
Mass adjusted for height$^{2.7}$, g/m$^{2.7}$	27.0 ± 4.8	24.8 ± 4.4	<0.001
CO adjusted for height$^{2.7}$, L/min/m$^{2.7}$	1.35 ± 0.24	1.30 ± 0.23	0.011
RV parameters			
EF, %	57.5 ± 8.1	56.8 ± 7.3	0.357
EDV, mL	132.8 ± 29.6	133.2 ± 28.2	0.866
EDV adjusted for height$^{2.7}$, mL/m$^{2.7}$	31.3 ± 6.5	31.6 ± 6.6	0.586
Female (n = 162)	n = 46	n = 116	
Age, years (mean, range)	56.2 (42–85)	54.7 (41–74)	0.269
LV parameters			
EF by volume, %	69.5 ± 6.0	68.1 ± 7.6	0.267
EDV, mL	110.1 ± 20.9	111.7 ± 23.9	0.704
Mass, g	79.7 ± 14.1	72.3 ± 14.3	0.004
Mass-to-volume ratio	0.74 ± 0.13	0.66 ± 0.12	0.001
CO, L/min	5.06 ± 1.07	4.84 ± 0.90	0.190
EDV adjusted for height$^{2.7}$, mL/m$^{2.7}$	31.4 ± 5.6	32.5 ± 6.5	0.315
Mass adjusted for height$^{2.7}$, g/m$^{2.7}$	22.7 ± 3.9	21.1 ± 4.1	0.022
CO adjusted for height$^{2.7}$, L/min/m$^{2.7}$	1.44 ± 0.26	1.41 ± 0.27	0.593
RV parameters			
EF, %	59.0 ± 7.6	61.0 ± 8.2	0.170
EDV, mL	99.1 ± 20.1	99.3 ± 19.3	0.957
EDV adjusted for height$^{2.7}$, mL/m$^{2.7}$	28.2 ± 5.6	28.9 ± 5.3	0.506

CO cardiac output, *EDV* end-diastolic volume, *EF* ejection fraction, *LV* left ventricle, *MS* metabolic syndrome, *RV* right ventricle

presence of preclinical cardiovascular states in asymptomatic individuals, such as SMI. Both MS and SMI were associated with LV concentric hypertrophy, but after adjusting for confounding factors, this relationship was no longer significant. The presence of SMI was independently associated with lower RV end-diastolic volume, while RVEF was preserved.

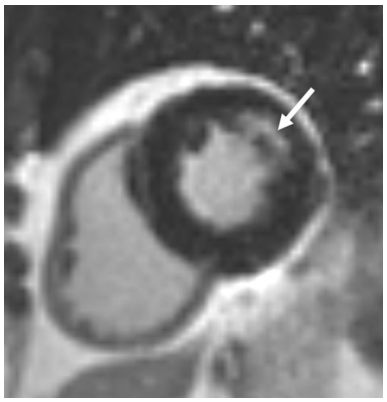

Fig. 3 Silent myocardial infarction as detected with MRI in a 70-year-old male with hypertension and smoking history. A patchy high intensity area (*arrow*) was found in the subendocardial zone of the anterolateral wall of the left ventricle on the late gadolinium-enhanced image

Association of cardiac mass and function with various cardiovascular risk factors

Higher LV mass was associated with higher BMI, SBP and current smoking. The Framingham study indicated that people with LV hypertrophy were more obese and had higher blood pressure as compared to those without [29], a finding supported by previous studies using cardiac MRI as well as the present study [9, 12]. It is well known that increased LV mass is of important prognostic value even in people without apparent CVDs [30]. In addition to LV mass, a high LV M/V (i.e., LV concentricity) is also clinically significant, as it can lead to ventricular dysfunction [31, 32] and has been demonstrated to be an independent prognostic indicator for non-heart failure cardiovascular events [25]. We found that a high LV M/V was related to high BMI, both SBP and DBP, TG, CRP and low eGFR, which suggests similar relationships to those observed in Caucasian and/or Hispanic populations [12, 33–36].

LVEDV was associated with BMI, both SBP and DBP and serum TG level in our study. In the MESA, however, high LDL cholesterol and high FPG, rather than high TG, were related to decreased LVEDV [9]. While LV cardiac output was associated with BMI, SBP and FPG, we found that LV systolic function as measured by LVEF was not associated with any of the examined CVD risk factors. In contrast, the MESA demonstrated that LVEF was associated with SBP and DBP, blood glucose and current smoking [9].

HDL cholesterol did not show significant associations with any of the examined ventricular parameters in our study. In agreement with our results, another cross-sectional study reported that there were no significant associations between LV parameters and HDL and non-HDL cholesterol levels [37].

High lipid and glucose levels were associated with decreased RVEDV, which is similar to the findings of the

MESA [8]. RV systolic function had a positive association with FPG and a negative association with increasing CRP, which was unique in our study.

Although cardiac function parameters were associated with various CVD risk factors, it should be noted that the variability explained by the regression models was small. Longitudinal studies are required to confirm whether this amount of variability is clinically significant from a long-term perspective.

Association of cardiac mass and function with metabolic syndrome

In this study, MS was associated with several cardiac abnormalities and the association differed between sexes. For example, MS was associated with higher LV mass (both unadjusted and adjusted for body size) and LV M/V in both sexes. However, when adjusted for its components, all of these associations lost their significance. This result may suggest that MS itself is not an independent risk factor of subclinical alteration of ventricular mass or function in Koreans. To the best of our knowledge, this is the first study to demonstrate that MS does not have an independent influence on cardiac mass and function when adjusted for other CVD risk factors, including its own effect on cardiac function on cardiac MRI.

Abnormalities in ventricular parameters in male subjects with silent myocardial infarction

The prevalence of SMI in our study population was 1.9%, far lower than the 17% (157 of 936 participants) observed in the ICELAND MI study [14] and 6.2% (114 of 1840 participants) observed in the MESA [17]. This is possibly explained by the younger age of our study population. The mean (±SD) age of our subjects was 55.0±7.0 years, whereas the median age (interquartile range) of the ICELAND MI study population was 76 (72–81) years and the mean age of the US cohort was 69 years. LV mass, both unadjusted and adjusted, and the LV M/V were significantly higher in male subjects with SMI. This was consistent with previous echocardiographic findings [38]. However, when adjusted for other CVD risk factors, all of these associations lost their significance. Schelbert et al. reported that patients with SMI not only had a higher LV mass, but also higher LVEDV (adjusted for body size) and lower LVEF [14]; however, we did not detect such a relationship. This difference might also be due to the younger age of our study population, which may have led to a shorter duration of myocardial infarction with a lesser extent of damage. Ethnicity may have contributed to this difference as well. We found that RVEDV (adjusted for body size) was lower in subjects with SMI even after adjustment for confounders. This is thought to be an incidental finding.

Diabetes mellitus is considered to be a CVD risk equivalent. The Framingham study has shown that both impaired glucose tolerance and diabetes are associated with increased coronary heart disease morbidity and mortality [39]. Previous studies reported that diabetic populations exhibit a high prevalence of SMI [14, 18]. In this study, diabetes was also suggested to be a risk factor for the development of SMI.

Limitations

This study did not include an adequate number of women; the number of men was three times higher than in the total study population. In particular, all of the subjects with SMI were male, so further studies of female subjects with SMI are needed. The number of SMI patients enrolled in the present study was also small.

Conclusion

Known CVD risk factors are associated with subclinical alterations in cardiac mass, geometry and function as measured by cardiac MRI in Korean subjects without clinical CVD. Subjects with preclinical cardiovascular conditions such as MS and SMI have concentric LV hypertrophy, but these conditions may not independently influence LV geometry or function. Diabetes may explain the etiology of SMI.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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