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Influence of Abdominal Circumference on the Inappropriateness of Left Ventricular Mass and Diastolic Function in Non-Obese Patients

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Abstract

Background and Objectives. Adipose tissue may be one of the sources of the humoral factors increasing left ventricular mass (LVM) via non-hemodynamic mechanisms. The involvement of visceral obesity in excessive or inappropriate LVM has not been established. We investigated the effect of abdominal circumference on the inappropriateness of LVM in non-obese patients.

Methods. Echocardiographic parameters for LVM and the indices for diastolic function were analyzed in 312 non-obese patients. Inappropriate LVM was defined as observed/predicted ratio (OPR) of LVM > 130%. Predicted LVM was calculated by the equation of $54.9 + 7.62 \times \text{height}(m^{2.7}) + 0.67 \times \text{stroke work} - 13.2 \times \text{sex}$ (male = 1, female = 2). Abdominal obesity was defined by abdominal circumference > 80 cm in females and > 90 cm in males.

Results. Multiple regression analysis showed abdominal circumference was a significant factor for OPR of LVM ($\beta = 0.256$) which was independent of age ($\beta = 0.215$), sex, systolic blood pressure ($\beta = -0.232$), body mass index ($\beta = 0.232$), and fasting blood glucose ($\beta = 0.146$). Odds ratio (OR) of abdominal obesity for inappropriate LVM was 3.28 (1.72–6.28), which was independent of age ≥ 55 [OR: 2.17 (1.11–4.25)], body mass index ≥ 22.5 kg/m^2 [OR: 2.24 (1.13–4.41)], and diabetes mellitus [OR: 2.27 (1.06–4.85)]. Age and sex adjusted abdominal circumference (86.4 ± 0.9 vs 82.1 ± 0.5), abdominal obesity (28.1% vs 54.1%), and metabolic syndrome (19.4% vs 51.6%) were higher in the inappropriate LVM group than the appropriate LVM group ($p < 0.001$).

Conclusions. Abdominal obesity or the presence of metabolic syndrome is an important factor to predict the inappropriateness of LVM even in non-obese patients.

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Key Words

■ **Obesity (body mass index)** ■ **Hypertrophy (left ventricular)**

INTRODUCTION

Left ventricular hypertrophy (LVH) is a well-known prognostic factor for cardiovascular events.[1] Left ventricular mass (LVM) is known to be influenced by hemodynamic factors such as blood pressure and stroke work as well as constitutional factors such as body size and sex.[2] Non-hemodynamic factors such as genetic traits, humoral factors and local tissue factors other than

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body size and sex may be involved in hypertrophy of the left ventricle.[3] The trophic effects of growth factors may be a cause of the inappropriateness of LVM. Adipose tissue may be one of the sources of the humoral factors related to LVH. Increased body mass index and insulin resistance were reported to be associated with LVH.[4,5] Appropriateness of LVM may represented by the percentage ratio of observed LVM to predicted LVM based on height, sex and stroke work. Inappropriateness of LVM is an independent prognostic factor regardless of the presence of LVH or not.[6] However, the involvement of abdominal obesity or metabolic syndrome in excessively or inappropriately increased LVM has not been established.[7]

This study was performed to investigate the effect of abdominal obesity on the inappropriateness of LVM, especially in non-obese patients.

SUBJECTS AND METHODS

The echocardiography database of 2,515 consecutive patients from December 1, 2004 to August 31, 2005 in Hanyang University Hospital, Seoul, Korea were analyzed in a cross-sectional design. During the study period, height, weight, abdominal circumference, blood pressure, and heart rate were measured before echocardiography. Abdominal circumference was measured at the mid-level between the iliac crest and lower costal margin with a spring-loaded measuring tape in the sitting or standing position. Duplicate measurements were made in all patients, and the average was used for analysis unless there was $< 3\%$ difference between duplicates, in which case the measurement was not used for analysis. The levels of total cholesterol, triglyceride, high-density lipoprotein (HDL), fasting blood glucose, and serum creatinine were gathered from the medical records.

All patients with echocardiography findings of wall motion abnormality, grade II or more valvular regurgitation, any valvular stenosis, pericardial disease, and poor M-mode measurements including interrogation angle of 10° or more were excluded. Patients with clinical heart failure or known cardiac disease history and hypertensive patients receiving antihypertensive medication were excluded. Patients with serum creatinine level greater than 1.5 mg/d*l* in males and 1.4 mg/d*l* in females were excluded. Among the remaining 951 patients compatible with these criteria, 585 patients with body mass index ≥ 25 kg/m^2 and 54 patients with incomplete laboratory data were excluded. Finally, 312 patients were included in this study. The study protocol was approved by the Institutional Review Board of Hanyang University Medical Center. Informed consent was acquired from each patient regarding the process of examination and use of the data.

Abdominal obesity is defined as abdominal circumference > 80 cm in females and > 90 cm in males with the Asia-Pacific perspective.[8] Metabolic syndrome was defined by Adult Treatment Panel III guideline for the other criteria.[9]

Echocardiography

Two-dimensional and guided M-mode echocardiography were performed on each subject by a single expert sonographer with a commercially available machine (IE-33, Philips) with a 1–5 MHz transducer. Measurements for M-mode guided calculations of LVM were taken at or just below the tip of the mitral valve with a paper speed of 50 mm/sec. At the time of the R wave uptake on electrocardiography minitoring, LV interventricular septal wall thickness (IVSTd), internal dimension (LVDd) and posterior wall thickness (PWTd) were measured from leading edge to leading edge according to the guidelines of the American Society of Echocardiography. LVM was calculated by the equation of $1.04 \times \{(\mathrm{IVSTd} + \mathrm{LVDd} + \mathrm{PWTd})^3 - \mathrm{LVDd}^3\} \times 0.8 + 0.6$.[10]

Doppler echocardiographic recordings were performed by pulsed-wave Doppler with the sample volume at the tip of mitral valve in the apical four-chamber view and recorded at a paper speed of 100 mm/sec. Early (E) and late (A) diastolic filling velocities, deceleration time (DT) and early to late velocity (E/A) ratio were determined as previously reported.[11] For patients below 55 years of age, impaired relaxation was diagnosed if there was E/A ratio $<$ or DT ≥ 240 msec. For older patients, both E/A ratio < 0.8 and DT ≥ 240 msec were required to diagnose impaired relaxation.[12]

Appropriateness of LVM

Appropriateness of LVM was expressed as observed/predicted ratio (OPR) of LVM.[3] Echocardiography data were obtained from 368 subjects (184 males, 184 females) with normal body mass index (below 25 g/m^2) and with normal blood pressure from the health screening program in a hospi-

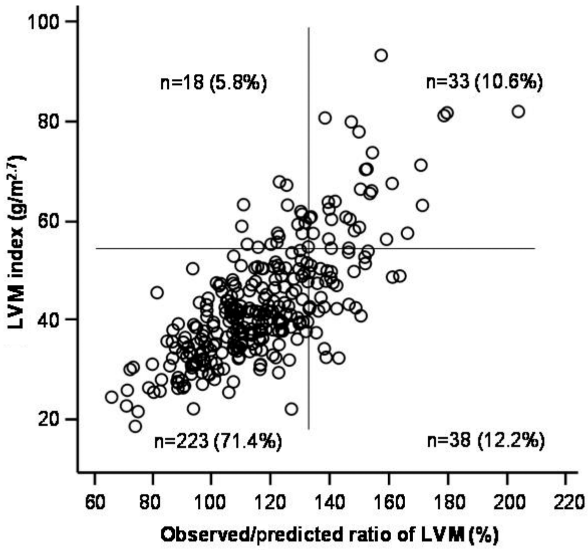

Fig. 1 Proportion of left ventricular mass according to the appropriateness and left ventricular hypertrophy
LVM = left ventricular mass.

tal ($n = 184$) and a rural community ($n = 184$) according to the previously described methods.[2)] LVMs indexed by body surface area were 93.1 ± 17.2 g/m^2 for males and 84.3 ± 14.5 g/m^2 for females. In this study, we adopted LVM indexed by height to highlight the effect of weight and the transformation of the height in meters to the power of 2.7 was most approximate to the linearity. LVMs indexed by height (m$^{2.7}$) were 38.9 ± 7.8 g/m$^{2.7}$ for male and 38.1 ± 7.5 g/m$^{2.7}$ for female. In a multiple regression model including stroke volume, sex, and height$^{2.7}$, LVM was predicted by the equation of 54.9 + 7.62 × height (m$^{2.7}$) + 0.67 × stroke work (g-m/beat) − 13.2 × sex (male = 1, female = 2) (constant = 54.9 ± 14.7 g, adjusted $R^2 = 0.576$, SEE = 21.67, $p = 0.001$). Age of the subject was 52.1 ± 16.2. The observed/predicted LVM was 99.9 ± 14.9% for males and 100.2 ± 15.2% for females.[13)]

We set the cut-off value (mean ± 2SD) for LVH as 54 g/m$^{2.7}$ for both sexes. The cut-off value between inappropriate LVM group and appropriate LVM group was 130% or higher for both sexes.

Statistical analysis

Data are expressed as mean ± SD. For the simple analysis of general characteristics and the sex difference, chi-square test and independent *t*-test were performed. Comparing the means between groups, age and sex were adjusted using least square means by the general linear model. For multiple comparisons between groups, Sidak confidence interval adjustment was added. For the numerical variables, the determinants of OPR were analyzed using a stepwise multiple linear regression model. The relationships of dichotomous categorical variables and inappropriate LVM were expressed as odds ratios with 95% confidence interval by stepwise multiple logistic regression analysis. All comparisons were 2-tailed, and $p < 0.05$ was considered to be statistically significant.

RESULTS

General characteristics of the subjects

Age of the subjects was 54.9 ± 13.0 years (range: 19−86 years). The female ratio was 159/312 (50.9%). Seventeen patients (5.4%) had hypertension, 46 (14.7%) had diabetes mellitus, 82 (26.2%) had metabolic syndromes, and 107 (34.3%) had abdominal obesity. Increased fasting blood glucose levels (≥ 110 mg/d*l*) were observed in 65 (20.8%) patients. Increased triglyceride levels (≥ 150 mg/d*l*) were observed in 73 (23.6%) patients. HDL level was less than 40 mg/d*l* (in males) or 50 mg/d*l* (in females) in 196 (62.8%) patients. Blood pressures were 130/85 mmHg or higher in 78 (24.8%) patients.

In 223 patients (71.4%), LV was normal regarding both the LVM index and the appropriateness. Among patients with apparently normal LVM index, 38 (12.2%) patients had inappropriate LVM. Among 51 LVH patients, 18 patients (5.8%) had appropriate LVH and 33 (10.6%) patients had inappropriate LVH (**Fig. 1**).

Abdominal obesity and inappropriate LVM were more frequent in females (15.9% vs 52.1%, 16.0% vs 29.3%, respectively; **Table 1**).

Factors determining OPR of LVM

In a simple correlation analysis, abdominal circumference had a significant correlation with OPR of LVM ($r = 0.376$, $p < 0.001$; **Fig. 2**). Regarding OPR of LVM, Pearson correlation coefficients of age ($r = 0.296$), female sex ($r = 0.202$), body mass index ($r = 0.351$), systolic blood pressure ($r = -0.159$), fasting blood glucose ($r = 0.236$), and triglyceride ($r = 0.167$) were also significant. Correlations between OPR of LVM and other parameters such as diastolic blood pressure ($r = -0.079$), heart rate ($r = -0.053$), serum

Table 1 General characteristics of the subjects

	Male (n=153)	Female (n=159)
Age (yr)	54.3±13.6	55.5±13.3
Height (cm)	169.0±5.9*	155.4±6.1
Weight (kg)	63.4±7.6*	53.8±6.1
Body mass index (kg/m^2)	22.2±2.2	22.3±2.1
Abdominal circumference (cm)	84.4±6.4*	82.0±9.1
Systolic blood pressure (mmHg)	122.3±14.5*	118.2±14.6
Diastolic blood pressure (mmHg)	78.6±9.6	76.8±12.1
Heart rate (beats/min)	70.1±13.3	70.3±12.1
Total cholesterol (mg/dl)	178.6±39.0*	193.5±39.8
Fasting blood glucose (mg/dl)	106.7±33.0	103.5±37.8
Creatinine (mg/dl)	1.09±0.18*	0.82±0.17
Triglyceride (mg/dl)	127.7±66.0	122.1±73.7
High-density lipoprotein (mg/dl)	39.5±12.9*	46.2±13.6
Metabolic syndrome	21.7%	30.6%
Abdominal obesity	15.9%*	52.1%
Fasting blood glucose (≥110 mg/dl)	26.0%*	15.9%
Triglyceride (≥150 mg/dl)	28.0%*	19.1%
High-density lipoprotein (<40/50 mg/dl in male/female)	60.7%	65.0%
Blood pressure ≥ 130/85 mmHg	30.8%*	19.2%
LVM index (g/m$^{2.7}$)	41.9±10.8	43.8±12.7
LVM index ≥ 54 g/m$^{2.7}$	13.3%	18.5%
Observed/predicted ratio of LVM (%)	110.4±19.1*	118.8±21.8
OPR of LVM ≥130%	16.0%*	29.3%
Impaired relaxation	12.1%	15.6%

Continuous values are mean±SD. *p<0.05 vs female.
OPR=observed/predicted ratio. Other abbreviation as in Fig. 1.

creatinine level ($r = 0.02$), total cholesterol ($r = -0.003$), and HDL ($r = -0.072$) were not significant. Partial correlation coefficient between abdominal circumference and OPR of LVM adjusted for age, sex, body mass index, fasting blood glucose level, systolic blood pressure, and triglyceride level was also significant (adjusted $r = 0.223$, $p < 0.001$).

In multiple linear regression analysis, abdominal circumference was a significant factor for OPR of LVM ($\beta = 0.256$, $p < 0.001$) which was independent of age ($\beta = 0.215$, $p < 0.001$), female sex ($\beta = 0.206$, $p < 0.001$), systolic blood pressure ($\beta = -0.232$, $p < 0.001$), body mass index ($\beta = 0.232$, $p < 0.001$), and fasting blood glucose ($\beta = 0.146$, $p = 0.004$).

In multiple logistic regression analysis, odds ratio (OR) of abdominal obesity for inappropriate LVM was 3.28 (1.72−6.28), which was independent of age ≥ 55 [OR: 2.17 (1.11−4.25)], body mass index ≥ 22.5 kg/m^2 [OR: 2.24 (1.13−4.41)], and the presence of diabetes mellitus [OR: 2.27 (1.06−4.85)]. Sex difference was not a significant factor for inappropriate LVM.

Comparison between appropriate LVM group vs inappropriate LVM group

Appropriate LVM was found in 77.2% ($n = 241$) of patients and inappropriate LVM in 22.8% ($n = 71$). Patients with inappropriate LVM were older (53.1 ± 13.4 vs 62.3 ± 10.9 yr, $p < 0.001$), more likely to be female, *i.e.* the proportion of female was 46.4% in the appropriate LVM group and 67.2% in the inappropriate LVM group ($p < 0.01$).

Age adjusted abdominal circumferences were higher in the inappropriate LVM group than appropriate LVM group in both males (83.7 ± 8.6 vs 87.8 ± 5.9 cm, $p = 0.004$) and females (80.9 ± 7.4 vs 84.2 ± 7.5 cm, $p = 0.04$; **Fig. 3**).

When adjusted for age and sex, abdominal obesity (28.1% vs 54.1%, $p < 0.001$) and metabolic syndrome (19.4% vs 51.6%, $p < 0.001$) were more frequent in the inappropriate LVM group than the appropriate LVM group. Adjusted fasting blood glucose (102.4 ± 25.9 vs 114.0 ± 58.8 mg/dl, $p = 0.02$) and triglyceride (119.6 ± 59.3 vs 142.3 ± 99.6 mg/dl, $p = 0.02$) levels were higher in the inappropriate LVM group than the appropriate LVM group. In subjects with inappropriate LVM, transmitral E/A was lower and impaired relaxation of LV was more frequent (**Table 2**).

DISCUSSION

In this study, we observed that abdominal obesity is a determinant of inappropriate increase of LVM even in patients regarded as non-obese by the criterion of body mass index, *i.e.* body mass index < 25 g/m^2. Moreover, its association with OPR of LVM is independent of body mass index. The presence of metabolic syndrome is also associated with inappropriate LVM. A previous study showed that increased body mass index and metabolic abnormality were associated with inappropriately increased LVM in hypertensive patients.[5] Abdominal obesity or insulin resistance was also demonstrated in hypertensive patients with LVH.[14] In our study, the frequency of metabolic syndrome paralleled the frequency of abdominal obesity in

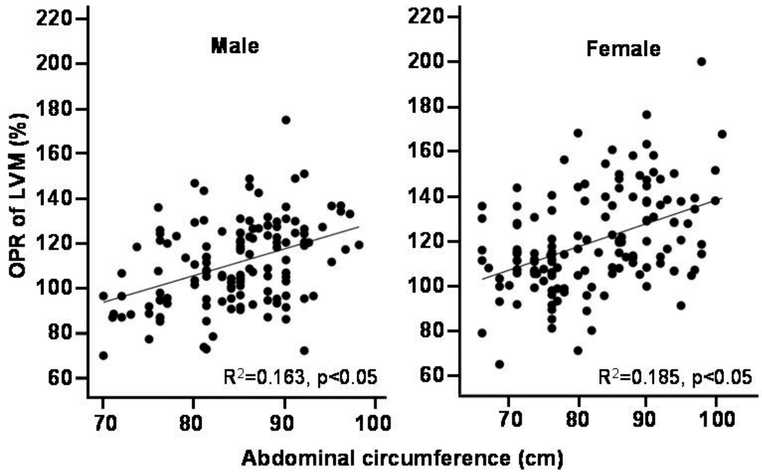

Fig. 2 Simple correlation between abdominal circumference and observed/predicted ratio of left ventricular mass
Abbreviations as in Fig. 1, Table 1.

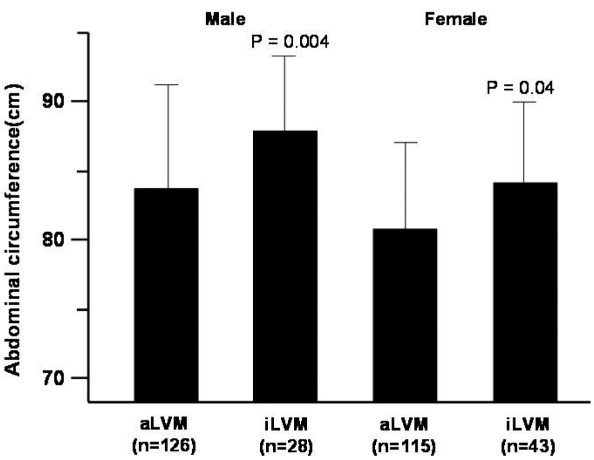

Fig. 3 Abdominal circumferences adjusted for age in appropriate LVM vs inappropriate LVM groups according to sex
aLVM = appropriate left ventricular mass; iLVM = inappropriate left ventricular mass.

the two groups.

The clinical significance of OPR of LVM may be explained by patients with inappropriate LVM with normal LVM index. In our study, the proportion of these patients was 53.5% ($n = 38$) among the patients with 71 inappropriate LVM.

These patients may be regarded as normal if we don't have the concept of appropriateness. Considering the fact that our study was done for relatively low risk subjects, the relationship between abdominal obesity and the inappropriately high LVM might be extended to apparently healthy subjects with normal body mass index.

For this study, treated hypertensive patients were excluded because the classes of antihypertensive

Table 2 Comparison between groups with appropriate LVM vs inappropriate LVM

	aLVM (n=241)	iLVM (n=71)
Age (yr)	53.1±13.4*	62.3±10.9
Female	115 (46.4%)*	43 (67.2%)
Body mass index (kg/m^2)	21.9±2.1*	23.1±2.1
Abdominal circumference (cm)	82.1±7.6*	86.4±7.9
Abdominal obesity (>90/80 cm in male/female)	64 (28.1%)*	42 (54.1%)
Systolic blood pressure (mmHg)	120.5±14.2	118.7±16.7
Diastolic blood pressure (mmHg)	78.1±10.9	76.1±11.4
Heart rate (beats /min)	69.9±12.7	70.8±12.3
Total cholesterol (mg/d*l*)	186.2±38.1	186.3±47.2
Fasting blood glucose (mg/d*l*)	102.4±25.9*	114.0±58.8
Creatinine (mg/d*l*)	0.89±0.19	0.91±0.21
Triglyceride (mg/d*l*)	119.6±59.3*	142.3±99.6
High-density lipoprotein (mg/d*l*)	43.5±13.6	40.6±13.6
High-density lipoprotein (<40/50 mg/d*l* in male/female)	62.4%	64.3%
Metabolic syndrome criteria number	1.59±1.1*	2.04±1.4
Metabolic sydrome (%)	48 (19.4%)*	33 (51.6%)
LVM index (g/m$^{2.7}$)	39.3±19.1*	52.8±28.7
Impaired relaxation (%)	29 (11.7%)*	38 (59.4%)
E/A	1.20±0.38 *	1.07±0.29
Deceleration time (msec)	203.1±39.7	203.8±46.4
Isovolumic relaxation time (msec)	76.2 ±7.6	78.3±8.1

Continuous values are mean±SD. *$p<0.05$ vs iLVM.
Abbreviations as in Figs. 1, 3.

medication may have differential effects on blood pressure lowering and regression of LVM.[15] The effects of antihypertensive drugs on the appropriateness of LVM have not been reported.

Impaired relaxation was more frequent in the inappropriate LVM group in our study. These results are comparable to the previous study done in hypertensive patients.[16] We used different criteria for the categorization of the transmitral flow parameters since it is greatly influenced by the aging process.

The inappropriate LVM group was older in our study. Age is not an independent determinant of LVM.[2] Abdominal obesity increases with aging, which suggests that the relationship of abdominal obesity and inappropriate LVM is usually compounded by age. After adjustment for age, we found that the relationship of abdominal obesity and inappropriate LVM was consistent and independent of the effect of age. Regarding the age factor, there is also another possibility that measurement errors may be exaggerated in the elderly. Abdominal obesity is a stronger predictor of insulin resistance than physical fitness in the elderly.[17] Abdominal circumference may be more important risk factor for death than body mass index.[18] These findings suggest that abdominal obesity may be one of the major factors associated with inappropriate LVM in the elderly. The functional aspect of abdominal obesity versus increased body mass index in the elderly needs more investigation.

Sodium retention may be one of the mechanisms of the inappropriateness of LVM. In our study, subjects with abnormal level were excluded, so serum creatinine was not associated with inappropriate LVM. However, renal dysfunction cannot be excluded as a contributor to inappropriate LVM until other more sensitive measurements, for example, cystatin C level or microalbuminuria are available.[19] Sodium retention possibly linked to insulin use may be one of the reasons why diabetes mellitus is associated with inappropriate LVM.

CONCLUSIONS

Abdominal obesity or the presence of metabolic syndrome is an important factor to predict early inappropriate increase of LVM even in non-obese patients.

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