CARDIOVASCULAR SCREENING IN ASYMPTOMATIC ADOLESCENTS WITH METABOLIC SYNDROME

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BACKGROUND: In recent days, the prevalence of childhood metabolic syndrome (MS) has increased substantially due to the increasing rate of childhood obesity on a global scale. The aims of this study were to detect the important parameters and provide the screening system to prevent cardiovascular disease in adolescents with MS.

METHODS: Ninety one male adolescents were divided into two groups based on the presence or absence of MS. Anthropometric measurement and laboratory study were studied. Intimal medial thickness and pulse wave velocity were estimated. Left ventricular mass index (LVMI), ejection fraction, myocardial velocity, strain and strain rate were measured by tissue Doppler imaging and strain rate imaging.

RESULTS: The prevalence of MS was 7.7%. Weight, body mass index (BMI), waist circumference (WC), glucose, insulin, homeostasis model assessment of insulin resistance, triglyceride and LVMI were significantly increased in the MS group. High density lipoprotein-cholesterol (HDL-C), peak early diastolic myocardial velocity (e'), systolic myocardial velocity (s') and global longitudinal strain were significantly lower in the MS group. In univariate analysis, LVMI was significantly correlated with BMI, WC, fat %, fat mass, systolic blood pressure, alanine aminotransferase, total cholesterol (TC) and low density lipoprotein-cholesterol. e' was significantly correlated with BMI, fat %, fat mass, and HDL-C. Global circumferential strain had significant correlation with glucose and TC. Basal anterolateral strain rate was significantly correlated with weight, BMI, WC, fat %, and fat mass.

CONCLUSION: LVMI, strain and strain rate are practical and accurate parameters for assessment of left ventricular function in adolescents with MS.

KEY WORDS: Metabolic syndrome · Adolescent · Tissue Doppler imaging · Strain rate.
stolic left ventricle (LV) function.\textsuperscript{28} Detection of myocardial deformation by TDI during the subclinical period in obese patients is important in clinical follow-up and in determining the prognosis.\textsuperscript{3-12}

Strain and strain rate imaging (SRI) have been proposed as a noninvasive echocardiographic technique to quantify regional myocardial function at rest and during acute and chronic ischemia.\textsuperscript{13-18} SRI is independent of cardiac rotational motion and a tethering effect.\textsuperscript{15}

There are several studies in adult with MS by strain and SRI. However, the results are controversial.\textsuperscript{16-19} The efficacy of strain and SRI has not been determined in adolescents with MS. There are limited data on subclinical LV systolic dysfunction in overweight and morbid obese children.\textsuperscript{29}

The aim of this study was to investigate cardiac structural and functional alterations in adolescents with MS and to compare those with control subjects to screen for MS in asymptomatic adolescents and to evaluate the impact of MS on global LV function by TDI and SRI.

**METHODS**

**STUDY POPULATION**

Ninety one healthy male adolescents aged between 14 and 15 participated in this study. They were divided into two groups based on the presence or absence of MS (MS group, non-MS group). Obesity was defined by body mass index (BMI) above the 95th percentile for age and sex as it is defined by Korean Centers of Disease Control and Prevention in 2007. People with endocrine dysfunction or other illnesses were excluded. We obtained informed consent from their guardians after explaining the procedure and purpose of the test thoroughly, and the study was approved by the Institutional Review Board of Ewha Womans University.

**DIAGNOSIS OF METABOLIC SYNDROME**

The diagnosis of MS was based on modified Cook's definitions (Table 1). In our study, the cut off value of fasting glucose was 100 mg/dL. MS was defined as having more than three components for their age and gender of the following metabolic abnormalities: abdominal obesity, [waist circumference (WC) ≥ 90 percentile], hypertriglyceridemia [serum triglyceride ≥ 110 (mg/dL)], low high density lipoprotein-cholesterol (HDL-C, < 40 mg/dL), high fasting plasma glucose (fasting plasma glucose ≥ 100 mg/dL), and high blood pressure (≥ 90 percentile (mm Hg)).

**ANTHROPOMETRIC MEASUREMENT**

We obtained anthropometric data of weight, height, WC, BMI, fat mass, and fat % from both groups. WC was measured with a tape-line at the mid-waist point between the lowest margin of the 12th rib and the mid portion of the superior iliac crest at minimal respiration. BMI was calculated by dividing the body weight in kilograms by height in meters. Fat mass and fat % were estimated by bioelectric impedance analysis (InBody 720, Biospace Co., Ltd., Seoul, Korea).

Blood pressure was measured using an automatic oscillometric method, Dinamap, Procare-200 (GE Medical System, Milwaukee, WI, USA) in a supine position after 10 minutes of adequate rest.

**LABORATORY MEASUREMENT**

Blood was drawn from all 91 adolescents, who had fasted for 14 hours prior to their blood sampling to determine the following parameters: blood glucose, total cholesterol (TC), HDL-C, low density lipoprotein-cholesterol (LDL-C), triglyceride (TG), aspartate aminotransferase, alanine aminotransferase (ALT). And, high sensitive C-reactive protein was also estimated.

Insulin resistance was measured by the homeostasis model assessment of insulin resistance (HOMA-IR), which was calculated by dividing the multiple of insulin (μU/mL) and serum glucose (mmol/L).

**ECHOCARDIOGRAPHIC PARAMETERS**

Echocardiography was performed using the IE33 machine (Philips Medical System, Andover, MA, USA) with an S5-1 transducer. Standard parasternal and apical views were acquired. Complete two-dimensional (2D) and M-mode echocardiogram, pulsed, color-flow Doppler, and TDI (Fig. 1) were obtained in the left lateral decubitus position. We measured the following LV parameters by M-mode echocardiography: interventricular septal wall thickness, posterior wall thickness, and LV end diastolic dimension at the chordae tendina level. The LV mass (LVM) and LV mass index (LVMI) were calculated. Ejection fraction (EF) was determined by using the bi-plane Simpson formula and fractional shortening was calculated using LV internal dimensions.

The diastolic function was assessed with pulsed Doppler mode from the apical window. Early diastolic (E), late atrial (A) peak velocities, E/A ratios, and deceleration time were performed using conventional pulsed wave Doppler echocardiography (Fig. 2).

To obtain longitudinal myocardial velocity, strain and strain rate with high quality, a narrow sector angle was used and im-

**Table 1. Definitions of metabolic syndrome in adolescents**

| Criteria |
|--------------------------|
| WC ≥ 90 percentile |
| SBP or DBP ≥ 90 percentile (mm Hg) |
| HDL-C < 40 mg/dL |
| Triglyceride ≥ 110 mg/dL |
| Fasting glucose ≥ 100 mg/dL |

WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, HDL-C: high density lipoprotein-cholesterol
Global strain was calculated as the average of the segments when six segments were measurable. Peak systolic strain rate was measured (Fig. 2).

Carotid intimal medial thickness cIMT was measured with an ultrasonogram to which a 12 MHz linear transducer was installed (CX50 machine; Philips Medical System, Andover, MA, USA). cIMT by an experienced technician unaware of the group to which the subject patients were assigned. The subject patients were given the test in a lying position with their head slightly turned. Within 1 cm from the junction of the right common carotid artery, the cIMT and vascular diameter of the vessel during the systolic and diastolic periods were measured. cIMT was defined as the distance between the intima and media layers.

A single investigator who was blinded to the clinical data performed. Circumferential strain curves from the short-axis view (six segments: anteroseptal, anterior, lateral, posterior, inferior, and septal) and longitudinal strain curves from the apical four-chamber view (six segments: basal interventricular septum, basal anterolateral, medium interventricular septum, medium anterolateral, apical septum, apical lateral septum).

Global strain was calculated as the average of the segments when six segments were measurable. Peak systolic strain rate was measured (Fig. 2).

**CAROTID INTIMAL MEDIAL THICKNESS**

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Asymptomatic Adolescents with Metabolic Syndrome

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The incidence of MS was 7.7% in 91 male healthy adolescents (Table 2).

The most common symptoms of the criteria were HDL-C < 40 mg/dL (100%), fasting glucose (85.7%), TG ≥ 110 mg/dL (71.4%), followed by WC ≥ 90 percentile (42.9%), systolic blood pressure (SBP) or diastolic blood pressure ≥ 90 percentile mm Hg (42.9%) (Table 3).

Comparison of anthropometric data

Weight, BMI, and WC were significantly higher in the MS group compared with the non-MS group (Table 4).

Comparison of biochemistry data

In the laboratory tests, glucose, insulin, HOMA-IR, and TG were significantly higher in the MS group compared with the non-MS group. HDL-C was significantly lower in the MS group compared with the non-MS group (Table 5).

Comparison of echocardiographic data

LVM was significantly higher in the MS group compared with the non-MS group (192.0 ± 73.0 g vs. 140.6 ± 30.2 g, p < 0.05, p < 0.05). LVMI were significantly higher in the MS group compared with the non-MS group (67.6 ± 22.3 g vs.

Table 2. Incidence of MS in the adolescents

| Criteria | Number | % |
|----------|--------|---|
| 0        | 28     | 30.8|
| 1        | 37     | 40.7|
| 2        | 19     | 20.9|
| 3        | 6      | 6.6 |
| 4        | 1      | 1.1 |

Table 3. Incidence of components of MS in obese adolescents

| Criteria | MS (-) (n = 84) | MS (+) (n = 7) |
|----------|-----------------|---------------|
| WC ≥ 90 percentile | 3 (3.6%) | 3 (42.9%) |
| SBP or DBP ≥ 90 percentile (mm Hg) | 7 (8.3%) | 3 (42.9%) |
| HDL-C < 40 mg/dL | 32 (38.1%) | 7 (100%) |
| Triglyceride ≥ 110 mg/dL | 9 (10.7%) | 5 (71.4%) |
| Fasting glucose ≥ 100 mg/dL | 29 (34.5%) | 6 (85.7%) |

Table 4. Comparison of anthropometric data between two groups

| Parameter  | MS (-) (n = 84) | MS (+) (n = 7) | p value |
|------------|-----------------|---------------|---------|
| Height (cm) | 165.1 ± 6.1     | 167.6 ± 6.1   | 0.298   |
| Weight (kg) | 57.1 ± 9.1      | 67.5 ± 12.8*  | 0.006   |
| BMI (kg/m²) | 20.9 ± 3.1      | 23.9 ± 3.6*   | 0.017   |
| WC (cm)     | 74.4 ± 8.9      | 81.7 ± 9.6*   | 0.038   |
| Fat (%)     | 17.7 ± 7.3      | 22.5 ± 7.6    | 0.101   |
| Fat mass (kg) | 10.6 ± 5.6    | 15.8 ± 7.7    | 0.026   |
| SBP (mm Hg) | 106.4 ± 11.4    | 120.0 ± 18.9  | 0.106   |
| DBP (mm Hg) | 58.4 ± 6.4      | 57.7 ± 3.5    | 0.777   |

*p value < 0.05. MS: metabolic syndrome, BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure.
with the non-MS group (1.71 ± 0.52 s\(^{-1}\) vs. 1.17 ± 0.64 s\(^{-1}\), \(p < 0.05\)) (Table 7).

**Intimal medial thickness and pulse wave velocity**

cIMT and pulse wave velocity were not significantly different between two groups (Table 8). The compliance and distensibility of the carotid artery were calculated. There was not any significant difference between two groups. Data is not shown.

**Linear correlation between cardiac parameters and other anthropometric data**

LVMI was significantly correlated with BMI (\(r = 0.39, p < 0.05\)), fat mass (\(r = 0.36, p < 0.05\)), SBP (\(r = 0.34, p < 0.05\)), fat % (\(r = 0.33, p < 0.05\)), WC (\(r = 0.32, p < 0.05\)), and weight (\(r = 0.31, p < 0.05\)).

e' was significantly correlated with BMI (\(r = -0.25, p < 0.05\)), fat mass (\(r = -0.23, p < 0.05\)), SBP (\(r = -0.22, p < 0.05\)), and WC (\(r = -0.21, p < 0.05\)).

**Table 5. Comparison of biochemical parameters in adolescents between two groups**

| Parameter          | MS (-) (n = 84) | MS (+) (n = 7) | \(p\) value |
|--------------------|----------------|---------------|-------------|
| Glucose (mg/dL)    | 97.6 ± 6.4     | 108.4 ± 4.2*  | 0.0001      |
| Insulin (mU/L)     | 9.2 ± 6.8      | 13.6 ± 4.9*   | 0.016       |
| HOMA-IR            | 2.3 ± 1.8      | 3.6 ± 1.2*    | 0.007       |
| AST (IU/L)         | 23.5 ± 6.2     | 20.3 ± 2.6    | 0.113       |
| ALT (IU/L)         | 16.5 ± 9.4     | 15.4 ± 3.6    | 0.553       |
| TC (mg/dL)         | 155.1 ± 31.4   | 159.6 ± 33.5  | 0.719       |
| LDL-C (mg/dL)      | 87.6 ± 25.4    | 96.6 ± 30.9   | 0.379       |
| HDL-C (mg/dL)      | 53.3 ± 10.8    | 45.0 ± 4.7*   | 0.021       |
| TG (mg/dL)         | 70.3 ± 45.4    | 117.3 ± 46.8* | 0.01       |
| hs-CRP (mg/L)      | 1.0 ± 1.4      | 0.7 ± 0.9     | 0.558       |

*\(p\) value < 0.05. MS: metabolic syndrome, HOMA-IR: homeostasis model assessment of insulin resistance, AST: aspartate aminotransferase, ALT: alanine aminotransferase, TC: total cholesterol, LDL-C: low density lipoprotein-cholesterol, HDL-C: high density lipoprotein-cholesterol, TG: triglyceride, hs-CRP: high sensitive C-reactive protein

**Table 6. Comparison of conventional echocardiographic and tissue Doppler imaging data between two groups**

| Parameter        | MS (-) (n = 84) | MS (+) (n = 7) | \(p\) value |
|------------------|----------------|---------------|-------------|
| EF (%)           | 68.1 ± 7.1     | 65.9 ± 5.8    | 0.428       |
| FS (%)           | 38.5 ± 5.5     | 36.7 ± 4.4    | 0.413       |
| LVM (g)          | 140.6 ± 30.2   | 192.0 ± 73.0* | 0.004       |
| LVMI (g/m²)      | 51.5 ± 10.4    | 67.6 ± 22.3*  | 0.003       |
| MV E (cm/sec)    | 101.2 ± 13.3   | 91.2 ± 13.2   | 0.059       |
| MV A (cm/sec)    | 46.7 ± 9.5     | 47.3 ± 12.6   | 0.886       |
| MV E/A           | 2.3 ± 0.5      | 2.0 ± 0.5     | 0.325       |
| MV E-DT (ms)     | 130.8 ± 28.6   | 153.3 ± 29.9  | 0.05        |
| e’ (cm/sec)      | 11.7 ± 2.1     | 10.1 ± 2.9*   | 0.033       |
| a’ (cm/sec)      | 6.8 ± 1.6      | 6.7 ± 1.9     | 0.811       |
| e’/a’            | 8.8 ± 1.8      | 9.1 ± 2.0     | 0.693       |
| s’ (cm/sec)      | 7.8 ± 1.2      | 6.6 ± 1.0*    | 0.014       |
| GLS (%)          | -19.5 ± 2.7    | -17.5 ± 2.0*  | 0.048       |
| GCS (%)          | -19.6 ± 3.8    | -19.4 ± 4.3   | 0.894       |
| LSR (BAL) (s\(^{-1}\)) | 1.5 ± 0.5 | 1.8 ± 0.5 | 0.23 |

*\(p\) value < 0.05. MS: metabolic syndrome, EF: ejection fraction, FS: fraction shortening, LVM: left ventricle mass, LVMI: left ventricle mass index, MV E: early diastolic velocity, MV A: late atrial peak velocity, DT: deceleration time, e’: peak early diastolic myocardial velocity, a’: peak late diastolic myocardial velocity, s’: systolic myocardial velocity, GLS: global longitudinal strain, GCS: global circumferential strain, LSR (BAL): longitudinal strain rate (basal anterolateral)

51.5 ± 10.4 g, \(p < 0.05\) (Table 6).

e’ was significantly lower in the MS group compared with the non-MS group (10.1 ± 2.9 cm/sec vs. 11.7 ± 2.1 cm/sec, \(p < 0.05\)). s’ was significantly lower in the MS group compared with the non-MS group (6.6 ± 1.0 cm/sec vs. 7.8 ± 1.2 cm/sec, \(p < 0.05\)). Global longitudinal strain (GLS) was significantly lower in the MS group compared with the non-MS group (-17.5 ± 2.0% vs. -19.5 ± 2.7%, \(p < 0.05\)) (Table 6).

There was a significant reduction in longitudinal strain at the LV medium anterolateral septum (-21.68 ± 7.00% vs. -13.28 ± 5.56%, \(p < 0.05\)), the medium interventricular septum (-23.82 ± 4.89% vs. -17.14 ± 3.18%, \(p < 0.05\)) and the apical anterolateral longitudinal septum (-16.77 ± 5.27% vs. -12.43 ± 4.86%, \(p < 0.05\)) (Table 7).

The longitudinal strain rate (LSR) was significantly lower in the medium interventricular septum in the MS group compared with the non-MS group (1.71 ± 0.52 s\(^{-1}\) vs. 1.17 ± 0.64 s\(^{-1}\), \(p < 0.05\)) (Table 7).

**Intimal medial thickness and pulse wave velocity**

cIMT and pulse wave velocity were not significantly different between two groups (Table 8). The compliance and distensibility of the carotid artery were calculated. There was not any significant difference between two groups. Data is not shown.

**Linear correlation between cardiac parameters and other anthropometric data**

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fat % (r = -0.22, p < 0.05), and fat mass (r = -0.21, p < 0.05).

Basal anterolateral LSR was significantly correlated with WC (r = 0.25, p < 0.05), fat mass (r = 0.24, p < 0.05), BMI (r = 0.22, p < 0.05), fat % (r = 0.21, p < 0.05), and weight (r = 0.26, p < 0.05) (Table 9).

**LINEAR CORRELATION BETWEEN CARDIAC PARAMETERS AND BLOOD CHEMISTRY DATA**

LVMI was significantly correlated with ALT (r = 0.34, p < 0.05), TC (r = 0.24, p < 0.05), and LDL-C (r = 0.20, p < 0.05). e’ was significantly correlated with HDL-C (r = 0.22, p < 0.05).

’s’ was significantly correlated with LDL-C (r = 0.23, p < 0.05). GLS was significantly correlated with insulin (r = 0.23, p < 0.05), HOMA-IR (r = 0.22, p < 0.05), and TG (r = 0.2, p < 0.05).

Global circumferential strain (GCS) was significantly correlated with glucose (r = 0.22, p < 0.05) and TC (r = 0.21, p < 0.05).
0.05) (Table 10).

**Linear correlation between insulin resistance and other parameters**

HOMA-IR was significantly correlated with GLS \((r = 0.22, p < 0.05)\) (Table 10).

**Discussion**

In our study, adolescents with MS showed subclinical LV systolic and diastolic dysfunction by TDI and SRI. LVM and LVMI were significantly higher in the MS group compared with the non-MS group. \(e', s'\) velocity and GLS were significantly lower in the MS group compared with the non-MS group. There was a significant reduction in strain at the LV medium anterolateral septum, the medium interventricular septum and the apical anterolateral longitudinal septum. The LSR was significantly lower in the medium interventricular septum in the MS group compared with the non-MS group.

**Table 9. Linear correlation between echocardiographic parameters and anthropometric data between two groups**

| Parameter | Height | Weight | BMI | WC | Fat % | Fat mass | SBP | DBP |
|-----------|--------|--------|-----|----|-------|----------|-----|-----|
| EF        | -0.09  | 0.05   | 0.08| 0.07| 0.08  | 0.07     | -0.03| -0.01|
| FS        | -0.12  | 0.01   | 0.03| 0.02| 0.03  | 0.05     | -0.06| -0.06|
| LVM       | 0.36*  | 0.57*  | 0.43*| 0.36*| 0.31* | 0.43*    | 0.28*| 0.02 |
| LVMI      | 0.04   | 0.31*  | 0.39*| 0.32*| 0.33* | 0.36*    | 0.34*| 0.09 |
| MV E      | -0.11  | 0.01   | 0.07| 0.08| 0.12  | 0.1      | 0.18 | 0.03 |
| MV A      | 0      | 0.08   | 0.11| 0.1 | 0.15  | 0.13     | 0.02 | 0.03 |
| E/A       | -0.04  | -0.05  | -0.05| -0.02| -0.05 | -0.05    | 0.06 | 0.01 |
| DT        | -0.04  | 0.02   | 0.01| 0.03| -0.04 | -0.04    | -0.09| -0.03|
| e'        | 0.12   | -0.17  | -0.25*| -0.17| -0.22*| -0.21*   | -0.05| 0     |
| a'        | 0.1    | 0.08   | 0.15| 0.13| 0.18  | 0.16     | 0.09 | 0.03 |
| E/e'      | -0.12  | 0.16   | 0.26*| 0.21*| 0.25* | 0.24*    | 0.16 | 0     |
| s'        | 0.01   | -0.12  | -0.09| -0.12| -0.06 | -0.07    | 0.07 | 0     |
| GLS       | 0.02   | 0.09   | 0.06| -0.01| 0     | 0.05     | -0.01| -0.08|
| GCS       | 0.06   | -0.09  | -0.11| -0.13| -0.08 | -0.08    | 0.04 | -0.02|
| LSR (BAL) | 0.08   | 0.26*  | 0.22*| 0.25*| 0.21* | 0.24*    | 0.19 | -0.01|

*p value < 0.05. BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, EF: ejection fraction, FS: fraction shortening, LVM: left ventricle mass, LVMI: left ventricle mass index, MV E: early diastolic velocity, MV A: late atrial peak velocity, DT: deceleration time, e': peak early diastolic myocardial velocity, a': peak late diastolic myocardial velocity, s': systolic velocity, GLS: global longitudinal strain, GCS: global circumferential strain, LSR (BAL): longitudinal strain rate (basal anterolateral)

**Table 10. Linear correlation between echocardiographic parameters and biochemical data between two groups**

| Parameter | Glucose | Insulin | HOMA-IR | AST | ALT | TC | LDL-C | HDL-C | TG |
|-----------|---------|---------|---------|-----|-----|----|-------|-------|----|
| EF        | -0.06   | 0.04    | 0.04    | 0.07| 0.04| 0.04| 0.08  | 0.04  | 0.08|
| FS        | 0.02    | 0.11    | 0.11    | 0.06| 0   | 0   | 0.06  | 0.01  | 0.1 |
| LVM       | 0.23*   | 0.15    | 0.15    | 0.12| 0.12| 0.28*| 0.09  | 0.1   | 0.01|
| LVMI      | 0.17    | 0.15    | 0.15    | 0.14| 0.14| 0.34*| 0.24* | 0.2*  | 0.12|
| MV E      | -0.18   | -0.11   | -0.13   | 0.18| 0.23*| 0.13| 0.19  | 0.03  | 0.01|
| MV A      | 0.03    | -0.02   | -0.01   | 0.2* | 0.09| -0.03| -0.05 | -0.01 | 0.05|
| E/A       | -0.15   | -0.08   | -0.1    | 0.08| 0.06| 0.09 | 0.15  | 0     | 0.03|
| DT        | 0.08    | 0.01    | 0.01    | 0   | -0.08| -0.09| -0.02 | 0.24* | 0.01|
| e'        | -0.12   | -0.19   | -0.18   | 0.03| -0.02| -0.02| -0.11 | 0.22* | -0.15|
| a'        | -0.09   | -0.01   | -0.03   | -0.01| 0.06| 0.09 | 0.14  | -0.11 | 0.14|
| E/e'      | -0.05   | 0.04    | 0.02    | 0.17| 0.18| 0.11 | 0.2*  | -0.18 | 0.1 |
| s'        | -0.03   | -0.17   | -0.17   | 0.09| -0.04| -0.14| 0.23* | 0.15  | -0.12|
| GLS       | 0.14    | 0.23*   | 0.22*   | 0.1 | -0.06| 0.09 | 0.13  | -0.11 | 0.2* |
| GCS       | 0.22*   | -0.07   | -0.05   | -0.07| -0.13| 0.21*| 0.14  | 0.09  | 0.02|
| LSR (BAL) | 0.06    | 0.01    | 0.01    | -0.13| 0.1 | 0.11 | 0.12  | -0.04 | 0.05|

*p value < 0.05. HOMA-IR: homeostasis model assessment of insulin resistance, AST: aspartate aminotransferase, ALT: alanine aminotransferase, TC: total cholesterol, LDL-C: low density lipoprotein-cholesterol, HDL-C: high density lipoprotein-cholesterol, TG: triglyceride, EF: ejection fraction, FS: fraction shortening, LVM: left ventricle mass, LVMI: left ventricle mass index, MV E: early diastolic velocity, MV A: late atrial peak velocity, DT: deceleration time, e': peak early diastolic myocardial velocity, a': peak late diastolic myocardial velocity, s': systolic velocity, GLS: global longitudinal strain, GCS: global circumferential strain, LSR (BAL): longitudinal strain rate (basal anterolateral)
Utility of TDI and SRI have not been determined in pediatric patients with MS.

Previous adult studies have investigated the LV functions in patients with MS, but there is not any consensus. Grandi et al. \(^{16}\) have described that only LV diastolic function is reduced in MS, although LV systolic function is normal. Masugata et al. \(^{17}\) also have reported that cardiac diastolic function was impaired in patients with MS even if they have neither LV hypertrophy nor systolic dysfunction. On the other hand, Wong et al. \(^{18}\) have found that MS is correlated with both LV systolic and diastolic dysfunction in subjects with significant risk factors but not with CVD. Those studies have provided valuable information about LV function in MS.

However, there are some limitations to compare our data with those studies, because our study was performed in adolescents, the other studies were done on adult age patients.

Diagnostic methods used to assess cardiac function are different between several studies. Gong et al. \(^{19}\) found that regional LV systolic and diastolic function were impaired in patients with MS by using strain and SRI.

The impairment was more serious in patients with four risk factors than in patients with three risk factors. This suggests that different components of MS may have synergistic effects on LV functions.

In our study, ventricular systolic and diastolic function were significantly lower in the MS group with more than 3 risk factors compared with non-MS group with less than 3 risk factors. These results were in accordance with the previous studies in adult groups. \(^{16}\)

Although the cause of altered LV function in MS is not fully understood, the components of MS may produce latent cardiac structural and functional disorders. MS is also related to LV hypertrophy and LV diastolic dysfunction. \(^{20}\)

In our studies, e’ velocity showed significant negative correlation with BMI, fat %, fat mass. e’ was significantly correlated with HDL-C.

GLS was significantly correlated with insulin, HOMA-IR and TG. GCS was significantly correlated with glucose and TC. Basal anterolateral LSR was significantly correlated with weight, WC, fat mass, BMI, and fat %. LVMi was significantly correlated with ALT and glucose.

Obesity is associated with increased metabolic demand because of greater adipose tissue, larger blood overload and increased preload to the heart. Also, vascular alterations of arterial stiffness and resistance increase afterload to the heart. Obesity can cause cardiac hypertrophy in systolic and diastolic cardiac dysfunction. \(^{21}\)

Obesity affects myocardial metabolism. Alterations in myocardial substrate metabolism have been related with reduced myocardial contractile dysfunction in insulin resistant patients and diabetes mellitus. \(^{19}\) LV abnormalities seem to be greater in visceral rather than in subcutaneous obesity. \(^{22}\) The cause of this myocardial dysfunction remains unclear, although chronic volume overload, insulin resistance, autonomic changes and metabolic abnormality have already been studied.

BMI, insulin resistance and duration of obesity are associated with cardiac dysfunction. \(^{23}\)

Increased adiposity is associated with insulin resistance because of the release of free-fatty acid, as well as actions of adipokines. Lipotoxicity can also contribute to cardiac myocyte apoptosis. \(^{19}\) Other possible mediators include the hormonal and cytokine release associated with obesity. Adiponectin is reduced in obesity, and this may induce insulin resistance. \(^{24}\)

Our results suggest that obesity contributes to the myocardial changes. Interestingly, we found that HOMA-IR was significantly positively correlated with GLS (r = 0.22). Hyperinsulinemia and insulin resistance have been known to cause an altered collagen/muscular ratio. \(^{25}\) Studies have demonstrated an accumulation of myocardiad collagen is related to interstitial and perivascular fibrosis, both of which is associated with LV early diastolic dysfunction. \(^{26}\)

In our study, LV hypertrophy, which was assessed by the LVMi was significantly different between patients with MS and those in control adolescents. LVMi was significantly correlated with BMI (r = 0.39), fat mass (r = 0.36), SBP (r = 0.34), fat % (r = 0.33), and WC (r = 0.32). LVMi was significantly correlated with ALT (r = 0.34), TC (r = 0.24), and LDL-C (r = 0.20).

Both eccentric and concentric hypertrophy have been noted in adults with obesity and are impacted by the degree and duration of the obesity. \(^{27}\) Altered cardiac morphology may be a precursor to impaired cardiac function. Studies on children and adolescents with obesity have reported changes in cardiac mechanics including diastolic dysfunction \(^{28}\) and systolic dysfunction at rest \(^{29}\) and during exercise. \(^{30}\)

Currently, it is uncertain how cardiac dysfunction will progress over time, and how cardiac dysfunction correlates to outcomes in adulthood. In adults, even with cardiac enlargement and systolic dysfunction, several studies have revealed that LVEF is normal in many obese subjects. \(^{31}\) Although the EF is normal, myocardial contractile abnormalities may still exist, and are more susceptible to measures by TDI and SRI analyses. \(^{32}\)

TDI is used to estimate LV filling pressures in obese subjects. The ratio of early diastolic filling to mitral annular tissue velocity (E/E1) is a well-established index of pulmonary capillary wedge pressure strain. \(^{33}\)

In our study, we performed the measurements to keep the angle between the ultrasound beam and the LV longitudinal axis as small as possible to eliminate errors and the data were averaged using a compound function to decrease noise by 2D speckle tracking imaging.

The traditional method of deriving regional systolic strain and strain rate from TDI is, however, limited by angle dependency.

We found that regional strain and strain rate reduction in the MS group with normal LVEF. The use of TDI and SRI analysis
could detect pre-clinical changes in LV regional systolic and diastolic dysfunction before conventional changes in EF.13

Previous studies of MS in children and adolescents, gave evidence on the clustering of risk factors for CVD.14 Although there hasn’t been any research that has shown the impact of MS on heart disease in childhood, some autopsy studies in childhood have shown that the factors of obesity, high blood pressure, high TG, and low HDL-C are related to the early stage of coronary atherosclerosis.15,16 Early identification of the clustering of risk factors in childhood is important in targeting efforts for chronic disease prevention.

There are several limitations to this study. This study only analyzed male subjects. There is also a lack of comprehensive assessment according to diverse growth and development because the age was confined to ages between 14 and 15 years old. Another limitation of this study includes the accuracy and reproducibility of measuring the parameters using echocardiography.

Further research on a larger adolescent population is needed, because there is no standard cut-points for parameters of MS. The longitudinal model design from adolescence to adulthood is needed to explore the complexity of MS risk factors. Since the time course of an adolescent to obesity and clinical disease is short, there is a lack of difference between the MS group and the non-MS group. The prospective and longitudinal studies may offer good opportunities in pediatric cardiovascular research.

In conclusion, in the present study, we have shown the presence of impaired global left ventricular function in patients with MS compared with control subjects without MS even if they have normal LVEF. This finding emphasizes the importance of early diagnosis and management of MS to prevent the progression of ventricular dysfunction to overt structural and symptomatic cardiac disease.

Early identification of regional and global LV functions by TDI and SRI in MS risk group may help to stratify risk and guide therapy. Because the components of the MS tended to be highly correlated with each other, it would be difficult to detect completely separate effects of each component. Strain and SRI would be a sensitive and feasible method to detect subclinical abnormalities in those populations.

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