

Evaluation of subclinical left ventricular dysfunction in overweight people with 3D speckle-tracking echocardiography

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ABSTRACT

Objective: Obesity is associated with cardiovascular risk factors and is a major predictor of cardiovascular disease and mortality. This global burden affects myocardial function by inducing structural and functional alterations. Although subclinical left ventricular (LV) dysfunction is known in obese subjects, there is not sufficient information about overweight people. The aim of the present study was to evaluate subclinical LV dysfunction in overweight people with three-dimensional speckle-tracking echocardiography (3D-STE).

Methods: One hundred eighteen consecutive patients between 18 and 80 years old were enrolled into the study. Patients were divided into three groups according to body mass index (BMI): normal (BMI: 18.5–24.9 kg/m²) (n=35), overweight (BMI: 25–29.9 kg/m²) (n=43), and obese (BMI ≥30 kg/m²) (n=40). 3D-STE was performed, and global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), and global area strain (GAS) were measured. 3D-STE results were compared between the groups.

Results: The mean age of the patients was 60.97±8.94 years, and 55.1% of the patient population were male. Mean GCS was –13.5, GLS was –11.9, GRS was 32.3, and GAS was –22. As BMI increased, GCS and all other strain parameters were significantly worse [p<0.001 (normal–overweight), p<0.001 (normal–obese), and p<0.001 (overweight–obese) for GCS, GLS, GRS, and GAS]. A positive linear correlation was observed between BMI and all measured strain parameters (r=0.673, p<0.001 for BMI and GCS).

Conclusion: 3D-STE is a non-invasive parameter to detect subclinical LV dysfunction, and global strain values are significantly correlated with BMI. Subclinical LV dysfunction was detected in overweight people in addition to obese subjects. (*Anatol J Cardiol* 2019; 21: 180-6)

Keywords: 3D speckle-tracking echocardiography, overweight people, subclinical left ventricular dysfunction

Introduction

Obesity and overweight have become a major health problem with dramatically rising trends in prevalence worldwide. This global burden is associated with cardiovascular risk factors and is a major predictor of cardiovascular disease and mortality (1-3). Obesity has different effects on hemodynamic and cardiovascular structures and functions. It increases total blood volume, cardiac output, and cardiac workload. Even independent of arterial pressure, obesity is characterized by increasing chamber dilation without marked increases in wall thickness, leading to eccentric left ventricular (LV) hypertrophy. All these alterations form part of the so-called “obesity cardiomyopathy” (4-6). Obese and overweight individuals have

significantly greater prevalence of LV diastolic dysfunction and higher risk of heart failure than individuals with normal weight (7, 8). Therefore, early recognition of subclinical myocardial dysfunction is important to preserve LV systolic functions and to prevent the development of “obesity cardiomyopathy”.

Echocardiography is the leading, non-invasive, inexpensive, and convenient cardiac imaging technique. Two-dimensional (2D) echocardiography is routinely used in clinical practice, but cannot detect early myocardial changes as long as there are no LV wall motion abnormalities and no reduction in left ventricular ejection fraction (LVEF).

During recent years, deformation imaging has advanced rapidly, and three-dimensional speckle-tracking echocardiography (3D-STE) has emerged as a valuable tool that provides

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a comprehensive and reliable assessment of myocardial function (9-11). It has been shown to be useful in the detection of subclinical LV dysfunction in patients with early-stage heart failure and hypertension (HT) (12, 13).

Myocardial deformation pathologies may occur in the early stages of LV systolic function impairment even if LVEF is measured in the normal range in 2D echocardiography. 3D-STE allows the assessment of subclinical myocardial damage by using strain parameters.

Although subclinical LV dysfunction is known in obese subjects, there is not sufficient information about overweight people. To the best of our knowledge, there is no study evaluating subclinical LV dysfunction in overweight patients with 3D-STE. As a result of this, we aimed to evaluate subclinical LV dysfunction in overweight subjects with 3D-STE.

Methods

Study population

One hundred eighteen consecutive patients between 18 and 80 years old were enrolled into the study between January 2016 and June 2016. Patients were divided into three groups according to body mass index (BMI): normal (BMI: 18.5–24.9 kg/m²) (n=35), overweight (BMI: 25–29.9 kg/m²) (n=43), and obese (BMI: ≥30 kg/m²) (n=40). Exclusion criteria were history of myocardial infarction, percutaneous coronary intervention, and coronary bypass grafting, valvular heart diseases, arrhythmia, cardiac pacemaker, heart failure, cardiomyopathy, segmental LV wall motion abnormalities, LVEF < 55%, left bundle branch block or right bundle branch block, thyroid dysfunction, chronic renal failure (glomerular filtration rate <60 mL/min/1.73 m²), peripheral artery disease (ankle brachial index < 0.9), malignancy and use of cardiotoxic medication, uncontrolled HT, congenital heart disease, and poor 3D image quality. The study was approved by the Local Ethics Committee. Informed consent was obtained from all of the patients included in the study.

Demographic and clinical evaluation of patients

HT was defined by a previous diagnosis of HT or the presence of systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg. Diabetes mellitus (DM) was defined as fasting plasma glucose ≥126 mg/dL or plasma glucose level ≥200 mg/dL for 2 h after the 75 mg oral glucose tolerance test or glycated hemoglobin ≥6.5% or patients using antidiabetic medications. Hyperlipidemia (HLP) was defined as total cholesterol >190 mg/dL or previous diagnosis of dyslipidemia. Cigarette smoking was defined as smoking ≥1 cigarettes/day for at least 1 year, without an attempt to quit.

Echocardiographic image acquisition and analyses

Baseline 2D and 3D echocardiographies were performed using a commercially available echocardiographic system

(Vivid E9; GE Healthcare, Horten, Norway) equipped with a 4 V phased-array matrix transducer (1.5-4.0 MHz). All images were accrued from patients in the left lateral decubitus position and connected to electrocardiography according to the echocardiography guidelines. The frame rate >25 fps was kept to work on 3D-STE. LVEF was measured automatically using 4D Auto LVQ. Stored raw data format images were exported to a separate workstation equipped with the 4D Auto LVQ package (Echo PAC v.110.1.3; GE Healthcare) for offline analysis of LV myocardial deformation. The software automatically detected the LV cavity endocardial border in 3D and provided the measured LV volumes. If the auto endocardial border detection was judged as inaccurate by the examiner, the LV endocardial borders were manually adjusted in multiplanar layout (three apical and three transverse planes) with a point-click method, immediately followed by secondary automated refinement of boundary detection according to the results. Following the assessment of the LV volumes and LVEF, an automatic trace of the epicardial border was displayed to identify the region of interest required for LV mass and myocardial deformation measurements. This epicardial trace was manually adjusted in order to include the entire LV wall thickness using the same point-click method. The strain parameters were calculated as global peak systolic strain. Global circumferential strain (GCS), global longitudinal strain (GLS), global radial strain (GRS), and global area strain (GAS) of the left ventricle were used for analyses.

Reproducibility

A total of 14 patients were randomly selected for the inter- and intraobserver variability analyses. Inter- and intraobserver agreements for GLS, GCS, GRS, and GAS were calculated. The intraclass correlation coefficients for interobserver comparisons of GLS, GCS, GRS, and GAS were 0.90 [95% confidence interval (CI), 0.88–0.94], 0.94 (95% CI, 0.92–0.96), 0.85 (95% CI, 0.83–0.90), and 0.95 (95% CI, 0.91–0.97), whereas the intraobserver comparisons were 0.86 (95% CI, 0.83–0.89), 0.94 (95% CI, 0.91–0.98), 0.91 (95% CI, 0.87–0.94), and 0.93 (95% CI, 0.86–0.97), respectively.

Statistical analysis

SPSS 25.0 (IBM Corp., Armonk, NY, USA) program was used for variable analysis. Before the analysis of the continuous variables, the normal distribution of the continuous variables with the normality test was tested by the Shapiro-Wilk test. Normally distributed continuous data are expressed as mean±standard deviation (minimum–maximum). Continuous variables that are not normally distributed are expressed as median (minimum–maximum). Categorical variables are expressed as n and percentages. For analysis of normally distributed data, one-way ANOVA and the common variables-corrected ANOVA (univariate ANOVA with covariates) were applied. For multiple comparison, Bonferroni (Dunn) test was used for simultaneous comparisons, and Dunnett's test was used for pairwise

comparisons. Continuous variables that are not distributed normally were analyzed by Kruskal–Wallis H test. Non-parametric Lilliefors-corrected Bonferroni test was used for multiple comparisons of the group median in these variables. Categorical variables were analyzed by Pearson chi-square analysis. Correlations between variables were analyzed by Pearson correlation analysis. Variables were examined at 95% confidence level. A p-value <0.05 was considered as statistically significant.

Results

The mean age of the patients was 60.97 ± 8.94 years, and 55.1% were male. Baseline characteristics of the study groups are compared in Table 1. Of all patients, 70.3% had HT, 34.7% had DM, and 56.8% were current smokers. The mean age of the overweight and obese groups was significantly higher than that of the normal group ($p=0.005$); however, no significant difference was found between the overweight group and the obese group in terms of mean age ($p=1.000$). Female gender was higher in the normal group than in the overweight and obese groups ($p=0.001$) (Table 1). There were no significant differences between the groups in history of HT, DM, HLP, and current smoking (Table 1). In addition, baseline SBP and DBP and LVEF were similar between the groups (Table 2).

The median triglyceride level was statistically higher in the obese groups than in both the normal and the overweight groups ($p=0.043$). In addition, the median high-density lipo-

protein cholesterol level was significantly lower in the obese group than in other groups ($p=0.004$) (Table 2).

Interventricular septum (IVS) thickness was significantly higher in overweight and obese subjects than in normal individuals ($p<0.001$). A significant increase in the IVS thickness was noted with an increase in BMI among the groups [$p<0.001$ (normal–overweight), $p<0.001$ (normal–obese), and $p<0.001$ (overweight–obese)] (Table 2).

3D-STE evaluation of LV function

Mean GCS was -13.5 , GLS was -11.9 , GRS was 32.3 , and GAS was -22 . GCS and all other strain values were significantly lower in overweight subjects than in normal subjects and also in obese subjects than in both normal and overweight subjects ($p<0.001$). As BMI increased, GCS and all other strain parameters were significantly worse [$p<0.001$ (normal–overweight), $p<0.001$ (normal–obese), and $p<0.001$ (overweight–obese) for GCS, GLS, GRS, and GAS] (Table 3, Fig. 1, 2). A positive linear correlation was observed between BMI and all measured strain parameters. In other words, strain parameters were found to be disrupted linearly as BMI increased ($r=0.673$, $p<0.001$ for BMI and GCS and $r=0.720$, $p<0.001$ for BMI and GLS) (Table 4).

It is known that age and sex can affect strain values. In our study, when the covariance analysis of strain values is corrected according to age and sex variables, age ($p=0.001$) and gender ($p=0.021$) were found to be effective for GLS variable, and age ($p=0.013$) was found to be effective for GAS variable.

Table 1. Patient characteristics

| | Normal (n=35) | Overweight (n=43) | Obese (n=40) | Total (n=118) | P-value |
|-------------------------------------|---------------------------------|-------------------------------|--------------------------------|-------------------------------|--------------------|
| Age ¹ | 56.49 ± 9.36 (33/78) | 62.70 ± 7.90 (39/86) | 63.03 ± 8.39 (40/80) | 60.97 ± 8.94 (33/86) | 0.001 ^a |
| Male gender ² | 10 (8.5) | 28 (23.7) | 27 (22.9) | 65 (55.1) | 0.001 ^b |
| Hypertension ² | 26 (74.3) | 27 (62.8) | 30 (75.0) | 83 (70.3) | 0.396 ^b |
| Diabetes mellitus ² | 10 (28.6) | 16 (37.2) | 15 (37.5) | 41 (34.7) | 0.658 ^b |
| Hyperlipidemia ² | 13 (37.1) | 22 (51.2) | 14 (35.0) | 49 (41.5) | 0.269 ^b |
| Smoking ² | 16 (45.7) | 24 (55.8) | 27 (67.5) | 67 (56.8) | 0.162 ^b |
| Systolic BP (mm Hg) ¹ | 122.74 ± 10.26 (105/139) | 121.88 ± 9.91 (98/139) | 123.65 ± 9.81 (100/139) | 122.74 ± 9.92 (98/139) | 0.724 ^a |
| Diastolic BP (mm Hg) ¹ | 75.34 ± 8.55 (58/89) | 77.84 ± 7.43 (59/91) | 79.05 ± 7.29 (60/89) | 77.51 ± 7.81 (58/91) | 0.115 ^a |
| Heart rate (beats/min) ³ | 67 (51/100) | 69 (46/105) | 69 (52/105) | 69 (46/105) | 0.676 ^c |

¹Data are expressed as mean±standard deviation (minimum–maximum).

²Data are expressed as n (%).

³Data are expressed as median (minimum–maximum).

^aP-values are shown as one-way ANOVA result for normally distributed variables.

^bP-values are shown as Pearson chi-square test result for categorical variables.

^cP-value is shown as Kruskal–Wallis H test result for non-normally distributed variable.

BP - blood pressure

Table 2. Echocardiographic and laboratory values*

| | Normal (n=35) | Overweight (n=43) | Obese (n=40) | Total (n=118) | P-value |
|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------|
| LVEF (%) | 62.37±3.50 (56/70) | 61.00±3.44 (55/67) | 61.08±3.63 (55/69) | 61.43±3.55 (55/70) | 0.174 ^a |
| Left atrium diameter (cm) | 3.47±0.43 (2.7/4.7) | 3.65±0.39 (3/4.6) | 3.54±0.38 (2.6/4.4) | 3.56±0.40 (2.6/4.7) | 0.154 ^a |
| IVS (cm) | 1 (0.8/1.2) | 1.1 (0.8/1.5) | 1.4 (0.9/1.6) | 1.15 (0.8/1.6) | <0.001 ^b |
| Creatinine (mg/dL) | 0.82 (0.51/4.3) | 0.86 (0.54/1.28) | 0.84 (0.5/1.4) | 0.85 (0.5/4.37) | 0.08 ^b |
| TC (mg/dL) | 202.83±37.41 (141/298) | 191.09±40.06 (118/279) | 212.28±47.92 (135/349) | 201.75±42.76 (118/349) | 0.076 ^a |
| TG (mg/dL) | 115 (63/353) | 114 (45/299) | 160 (68/669) | 124 (45/669) | 0.043 ^b |
| LDL-C (mg/dL) | 117 (69/187) | 117 (60/184) | 126 (74/252) | 120 (60/252) | 0.277 ^b |
| HDL-C (mg/dL) | 47 (31/109) | 47 (27/73) | 39.5 (25/75) | 45.5 (25/109) | 0.004 ^b |
| Uric acid (mg/dL) | 4.9 (2.7/8) | 5.4 (2.2/8.6) | 5.4 (2.9/8.7) | 5.2 (2.2/8.7) | 0.193 ^b |
| WBC (K/μL) | 6450 (4370/13180) | 6930 (4610/13560) | 7560 (4320/14740) | 7205 (4320/14740) | 0.045 ^b |
| Neutrophil (K/μL) | 3800 (1500/9500) | 4050 (1920/10520) | 4780 (2280/11020) | 4195 (1500/11020) | 0.025 ^b |
| Platelet (×1000) (K/μL) | 253 (168/465) | 240 (138/428) | 248.5 (151/515) | 247.5 (138/515) | 0.208 ^b |
| MPV (fL) | 10.93±1.12 (7.6/13) | 10.98±1.22 (8.3/14.1) | 10.78±0.99 (8.6/13.8) | 10.90±1.11 (7.6/14.1) | 0.685 ^a |

*Data are expressed as mean±standard deviation (minimum–maximum) for normally distributed continuous variables, and for non-normally distributed continuous variables, data are expressed as median (minimum–maximum).

^aP-values are shown as one-way ANOVA results for normally distributed variables.

^bP-values are shown as Kruskal–Wallis H test results for non-normally distributed variables.

LVEF - left ventricular ejection fraction; IVS - interventricular septum; TC - total cholesterol; LDL-C - low-density lipoprotein cholesterol; HDL-C - high-density lipoprotein cholesterol; TG - triglyceride; WBC - white blood cell; MPV - mean platelet volume

Table 3. Comparison of strain results between the groups*

| | Normal (n=35) | Overweight (n=43) | Obese (n=40) | Total (n=118) | P-value |
|-----|-----------------------|-----------------------|-----------------------|-----------------------|---------------------|
| GCS | -17±4.08 (-22/-11) | -14±3.46 (-19/-3) | -9 ±2.47 (-20/-4) | -13.5±4.37 (-22/-3) | <0.001 ^b |
| GLS | -16.69±2.37 (-22/-9) | -11.37±2.56 (-16/-5) | -8.33±2.69 (-16/-2) | -11.92±4.21 (-22/-2) | <0.001 ^a |
| GRS | 42.20±8.15 (25/63) | 30.47±6.65 (16/43) | 25.75±6.89 (12/40) | 32.35±9.81 (12/63) | <0.001 ^a |
| GAS | -28.37±3.77 (-38/-20) | -20.79±4.07 (-28/-13) | -17.98±4.33 (-29/-10) | -22.08±5.88 (-38/-10) | <0.001 ^a |

*Data are expressed as mean±standard deviation (minimum–maximum) for normally distributed continuous variables, and for non-normally distributed continuous variables, data are expressed as median (minimum–maximum).

^aP-values are shown as one-way ANOVA results for normally distributed variables.

^bP-values are shown as Kruskal–Wallis H test results for non-normally distributed variables.

Note: Multiple comparisons of group means for ANOVA test results were performed by parametric Bonferroni and Dunnett's tests. Multiple comparisons of group medians for Kruskal–Wallis H test were performed by Lilliefors-corrected non-parametric Bonferroni test.

GCS - global circumferential strain; GLS - global longitudinal strain; GRS - global radial strain; GAS - global area strain

Discussion

Although subclinical LV dysfunction was known in obese subjects, there was not enough information about overweight people. Overweight is an important step in the process leading

to obesity. Therefore, management of overweight patients and recognition of subclinical LV dysfunction at early stage are important. The present study has suggested that resting 3D-STE is a good clinical tool for detecting subclinical LV dysfunction in overweight patients with normal LVEF.

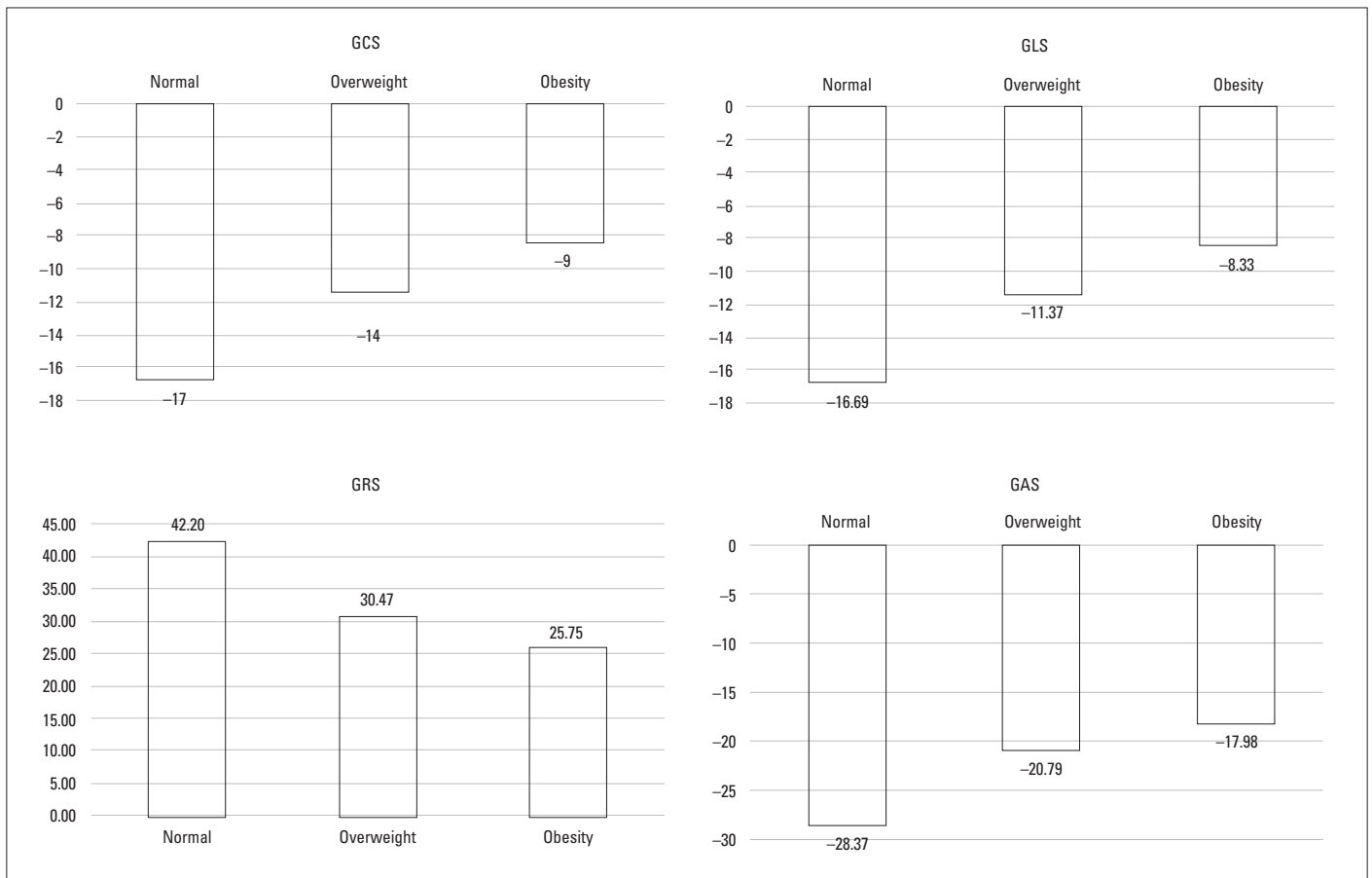


Figure 1. Comparison of strain results between the groups

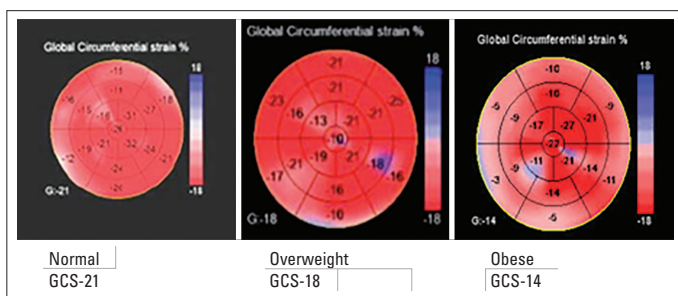


Figure 2. GCS worsened as BMI increases

Conventional 2D echocardiography is not a reliable technique to detect subclinical myocardial dysfunction. The most commonly used methods are checking for regional wall motion anomalies or LVEF. These methods have several limitations that are operator dependent, subjective, and calculating LVEF using Simpson’s method uses geometric assumptions. Previous studies had shown that LVEF is not a sensitive marker for subclinical dysfunction (14). Similar to previous studies, in the present study, there were no significant differences between the groups in terms of LVEF ($p=0.174$).

Strain imaging may help in detecting subclinical LV dysfunction. Previously, most 2D-STE was used for that aim. However, 2D-STE has also some limitations. It needs longer examination

Table 4. Correlation between BMI and strain parameters, IVS, and HDL-C

| | BMI | |
|-------|--------|--------|
| | r | P |
| GCS | 0.673 | <0.001 |
| GLS | 0.720 | <0.001 |
| GRS | -0.593 | <0.001 |
| GAS | 0.650 | <0.001 |
| IVS | 0.631 | <0.001 |
| HDL-C | -0.250 | 0.008 |

Partial correlation test r: correlation coefficient.
GCS - global circumferential strain; GLS - global longitudinal strain; GRS - global radial strain; GAS - global area strain; IVS - interventricular septum; HDL-C - high-density lipoprotein cholesterol; BMI - body mass index

times, uses geometric assumptions, and had a risk of mis-tracking of speckles out of the scanning plane. 2D strain suffers for the intrinsic limitations of 2D imaging, which prevents a full assessment of the complex myocardial deformation, for radial and circumferential strains in particular. 3D-STE, with the potentials to overcome these limitations, provides a more

accurate and convenient assessment in this clinical setting (15, 16). Kibar et al. (17) reported that 2D strain imaging parameters appear to be related to the severity of obesity, but their study has the expected limitations of 2D-STE, such as miss-tracking and angle dependence. Monte et al. (18) showed that geometrical and structural ventricular remodeling negatively influences deformational properties of the LV in obese subjects without cardiovascular risk factors. A significant reduction in longitudinal (GLS), radial (GRS), and area strain (GAS) was observed in the obese group ($p=0.001$ for all), whereas circumferential mechanic (GCS) was not different between the obese and the control groups (18). In our study, overweight people were also evaluated for subclinical myocardial dysfunction, and it was found that as BMI increased between the groups, all strain results were significantly worse ($p<0.001$ for GCS, GLS, GRS, and GAS).

Caputo et al. (19) aimed to investigate the potential influence of overweight on LV and atrial function, as assessed by 2D speckle-tracking strain analysis. They found that global peak atrial longitudinal strain was similar in the overweight and normal groups, whereas global peak ventricular longitudinal strain was significantly lower in the overweight group than in the normal weight group (19). However, they did not mention other strain values (CS, AS, and RS) in their studies. In addition, their study has the expected limitations of 2D-STE.

Study limitations

The main limitation of our study is small patient population (118 patients) and cross-sectional study design. Since there is no follow-up in our study, it is not possible to determine the importance of this result in daily practice. Further studies are needed to determine the real diagnostic and prognostic roles of these abnormalities in the clinical management of overweight patients.

Conclusion

In the present study, we determined that as BMI increased, myocardial function deteriorated. Subclinical LV dysfunction was detected in overweight people in addition to obese subjects. To the best of our knowledge, this is the first study that evaluates the utility of 3D-STE to point out preclinical myocardial abnormalities in overweight patients.

Our result supports that overweight people may have subclinical myocardial dysfunction even though they are apparently healthy and have a risk for cardiovascular events as well as obese subjects.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – M.D.; Design – M.D., S.K.; Supervision – E.V.; Fundings – None; Materials – M.D.; Data collection &/or processing – M.D.; Analysis &/or interpretation – M.D., S.K., E.V.; Literature search – M.D., S.K.; Writing – M.D., S.K.; Critical review – E.V.

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