

Subclinical left ventricular systolic dysfunction in patients with metabolic syndrome: A case-control study using two-dimensional speckle tracking echocardiography

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Original Article

Abstract

BACKGROUND: The dramatic increase in the prevalence of metabolic syndrome is associated with more increased cardiovascular morbidity and mortality in this group. Some recent studies suggested that metabolic syndrome is associated with increased risk of subclinical left ventricular (LV) systolic dysfunction. In the present cross-sectional case-control study, the utility of two-dimensional speckle tracking echocardiography (STE) was examined to detect early LV systolic dysfunction in this population.

METHODS: A total of 75 clinically asymptomatic subjects with left ventricular ejection fraction (LVEF) $\geq 55\%$, 39 without metabolic syndrome and 36 with metabolic syndrome, matched for gender and age, were enrolled in this case-control study. Metabolic syndrome was diagnosed using the National Cholesterol Education Program/Adult Treatment Panel III criteria. LV systolic function was assessed by STE-derived global and segmental longitudinal strain (ϵ_{LL}).

RESULTS: Global ϵ_{LL} was significantly lower in patients with metabolic syndrome compared with normal population ($-18.41 \pm 2.20\%$ vs. $-21.2 \pm 2.1\%$, $P < 0.001$). Segmental ϵ_{LL} was significantly lower in patients with metabolic syndrome in comparison to control group except for basal anteroseptal ($-19.95 \pm 2.90\%$ vs. $-21.15 \pm 3.30\%$, $P = 0.106$), basal anterolateral ($-17.5 \pm 5.0\%$ vs. $-18.3 \pm 4.1\%$, $P = 0.437$), and basal inferolateral segments ($-18.1 \pm 6.3\%$ vs. $-18.9 \pm 4.1\%$, $P = 0.526$).

CONCLUSION: STE-derived longitudinal LV strain (ϵ_{LL}), a marker of subclinical cardiovascular disease, is impaired in asymptomatic individuals with metabolic syndrome and normal LVEF.

Keywords: Metabolic Syndrome, Two-dimensional Echocardiography, Systole, Ventricular Dysfunction, Asymptomatic Disease

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Introduction

Metabolic syndrome is the concurrence of multiple metabolic abnormalities associated with the development and progression of atherosclerosis,¹ and generally, is diagnosed by the presence of three or more of the following conditions: obesity, insulin resistance, glucose intolerance, dyslipidemia, and hypertension.² The dramatically increasing prevalence of the metabolic syndrome, associated with the substantial increase in obesity and diabetes, is, therefore, an important public health concern.³

The most conventional tool in echocardiographically quantifying systolic left ventricular (LV) function is the ejection fraction (EF). However, measurement of EF is a simplistic approach, closely correlated to the radial component of myocardial deformation and thus limited by the

need for the geometric assumption. As a consequence, subtle changes in myocardial systolic function may be neglected in high-risk subclinical patients with metabolic syndrome when they are only assessed by EF in clinical practice. Novel quantitative techniques such as speckle-tracking echocardiography (STE) and tissue-Doppler imaging (TDI) can reliably measure LV strain which has a more sensitive diagnostic potential.⁴⁻⁶

Up to now, a few echocardiography-based studies has focused on subclinical cardiovascular disease in patients with metabolic syndrome using several parameters including more reproducible newer ones such as Tei index and TDI.^{7,8} Recently, LV myocardial strain has also been assessed by STE to determine the subclinical systolic effects of metabolic syndrome.⁹

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The purpose of this study was to evaluate the use of STE to assess LV myocardial strain as a marker of LV systolic dysfunction in asymptomatic population with metabolic syndrome and left ventricular ejection fraction (LVEF) $\geq 55\%$ to fortifying data to introduce a non-invasive accurate tool for screening of subclinical LV systolic dysfunction in patients with metabolic syndrome.

Materials and Methods

This case-control study was approved and performed in accordance with the regulations of the University's Institutional Review Board (Shiraz University of Medical Sciences, Shiraz, Iran) enrolling outpatient individuals aged between 35 and 55 with metabolic syndrome who were referred to the Shiraz Healthy Heart House* from April 2014 to December 2014. The patients were labeled to be affected by metabolic syndrome according to the updated National Cholesterol Education Program/Adult Treatment Panel III (NCEP ATP III) criteria for Asians. The subjects had to meet at least 3 of the following components: waist circumference ≥ 80 cm in women and ≥ 90 cm in men, fasting triglycerides > 150 mg/dl (≥ 1.7 mmol/l) or specific medication, high-density lipoprotein cholesterol < 40 mg/dl (< 1.03 mmol/l) for men or < 50 mg/dl (< 1.29 mmol/l) for women or specific medication, blood pressure $\geq 130/85$ mmHg or current use of antihypertensive medications, or fasting plasma glucose ≥ 100 mg/dl (≥ 5.6 mmol/l) or previously diagnosed Type 2 diabetes.¹⁰ Blood pressure was obtained from the upper arm of the patient who stopped smoking $\frac{1}{2}$ hour before, seated quietly in a chair with back support, with both feet flat on the floor for at least 5 minutes prior to measurement using a calibrated Beurer® Sphygmomanometer. Waist circumference was measured midway between the lower limit of the rib and iliac crest with the subject standing using a flexible tape.

Concomitantly, age and sex-matched individuals were selected from normal population to participate in the control group. The overt ischemic heart disease was excluded in all participants according to current symptoms, previous history of coronary artery disease, presence or absence of pathologic Q waves in at least 2 adjacent leads on resting 12-lead electrocardiogram (EKG) and LVEF $< 55\%$. The patients with bundle branch block in EKG, valvular heart disease, congenital heart disease, cardiomyopathies, and chronic kidney disease were

also excluded from the study.

To reach the study power of 80% and the effect size of 76% for the longitudinal LV strain (ϵ_{LL}) according to the same previous study,⁹ the sample volume was estimated to be at least 35 participants in each group. The random digit dialing method was used for sampling, and the excluded individuals were substituted by others who met the eligibility inclusion criteria. The two groups were matched for age and gender.

All participants underwent a two-dimensional (2D) transthoracic echocardiography including TDI and STE using a vivid E9 system and all echocardiographic measurements were performed by one echocardiologist according to the latest recommendations of the American Society of Echocardiography.¹¹ The LVEF was calculated by Simpson's biplane method, and the ϵ_{LL} (%) was calculated as the change in regional length relative to the length at end-diastole; $\epsilon_{LL} = (L_t - L_0) \times 100/L_0$, in which L_t is the length at time t and L_0 is the length of the segment at the beginning of the QRS complex. On 2D echocardiography, global ϵ_{LL} describes the relative length change of the LV myocardium between end-diastole and end-systole. After optimizing image quality, maximizing frame rate and minimizing foreshortening, peak mid-wall segmental and global ϵ_{LL} measurement was taken in the three standard apical views and averaged by automated function imaging application and demonstrated in Bull's eye (Figure 1).

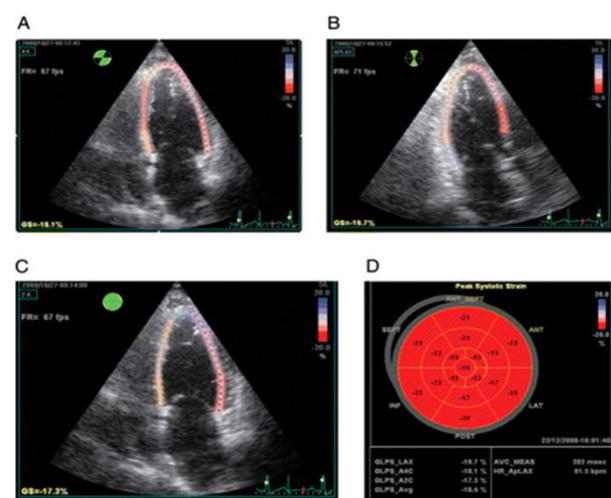


Figure 1. Representation of longitudinal strain. Apical (a), 4-chamber, (b) 3-chamber, (c) 2-chamber views and (d) Bull's-eye map showing segmental ϵ_{LL}

Using Kolmogorov-Smirnov test, the normal pattern of data distribution in measured

parameters was confirmed and therefore for comparison of data in case and control groups, the independent sample t-test and chi-square test were used for continuous and categorical variables, respectively. All continuous variables were expressed as mean \pm standard deviation, and categorical variables were expressed as number (n) and percentage (%). All collected data were analyzed by SPSS software (version 18.0, SPSS Inc., Chicago, IL, USA), and a $P < 0.050$ was considered statistically significant.

Results

A total of 75 eligibility criteria met individuals participated in the study from which 36 patients had metabolic syndrome and concomitantly, 39 age and gender-matched individuals from the normal population were examined echocardiographically in the control group.

The mean age of people in case and control groups was 40 ± 8 and 38.7 ± 8.9 , respectively ($P = 0.509$). For patients with metabolic syndrome, the distribution of gender was equal and 19 participants (48.7%) in control group were male in comparison with 20 (51.3%) females. Therefore, no statistically significant difference was present between case and control groups regarding age and gender. The clinical and demographic characteristics of participants are summarized in table 1.

Global ϵ_{LL} was significantly lower in patients with metabolic syndrome compared with normal population ($P < 0.001$) (Table 2) providing an effect size of 90%. In individuals with metabolic syndrome, although global ϵ_{LL} was slightly higher in women, there was no statistically significant difference between men and women (-17.88 ± 1.80 vs. -18.9 ± 2.5 ;

$P = 0.157$). Segmental ϵ_{LL} was significantly lower in patients with metabolic syndrome in comparison to control group except for basal anteroseptal, basal anterolateral and basal inferolateral segments ($P = 0.106, 0.437$ and 0.526 , respectively).

Discussion

In this cross-sectional, case-control study, the subclinical LV systolic dysfunction was focused which then revealing metabolic syndrome, as defined by NCEP ATP III criteria for Asians, was associated with reduced myocardial systolic function as indicated by an impaired global and segmental ϵ_{LL} in a sample of participants with metabolic syndrome signifying the need for a sensitive screening tool for asymptomatic LV systolic dysfunction and probably other subclinical aspects of cardiovascular disease in patients with metabolic syndrome according to its evolving prevalence and the hazardous potential of each of its components which in turn translated to a greater risk of cardiovascular disease.^{12,13} The results of this study are in concordance with such previous ones. For instance, Wang et al. showed that regional LV myocardial systolic function using strain and strain-rate imaging in patients with metabolic syndrome with normal LVEF was partly impaired and were negatively correlated with blood pressure, waist circumference, fasting plasma glucose and uric acid.¹⁴ Strain and strain-rate imaging were also used in a study on Chinese participants with metabolic syndrome revealing TDI as a sensitive and feasible method to detect subclinical abnormalities in such population;⁸ however, strain measured by using TDI has some limitations such as poor reproducibility, angle dependency, and signal noise.¹⁵

Table 1. The clinical and demographic characteristics of individuals with metabolic syndrome and control group

Variables	With metabolic syndrome (n = 36)	Without metabolic syndrome (n = 39)	P
Age (year) (mean \pm SD)	40.00 \pm 8.00	38.70 \pm 8.90	0.509
BMI (kg/m ²) (mean \pm SD)	33.20 \pm 3.60	26.60 \pm 4.00	< 0.001
Waist circumference (cm) (mean \pm SD)	96.31 \pm 10.45	80.40 \pm 9.67	< 0.001
Fasting TGs (mg/dl) (mean \pm SD)	156.00 \pm 16.98	92.87 \pm 13.00	< 0.001
HDL-cholesterol (mg/dl) (mean \pm SD)	46.80 \pm 5.00	52.82 \pm 6.40	< 0.001
Blood pressure (mmHg) (mean \pm SD)	140.00 \pm 13.00	132.00 \pm 11.50	0.006
Fasting plasma glucose (mg/dl) (mean \pm SD)	111.00 \pm 15.84	94.00 \pm 13.70	< 0.001
Any lipid-lowering medication [Yes (%)]	15 (41.7)	6 (15.4)	0.022
Previously diagnosed Type 2 diabetes [Yes (%)]	10 (27.8)	6 (15.4)	0.304
Gender (Female) [n (%)]	18 (50.0)	20 (51.3)	0.905
Any antihypertensive medication [Yes (%)]	14 (38.9)	7 (17.9)	0.077

The independent t-test and chi-square test were used for comparison of continuous and categorical variables, respectively. $P < 0.050$ was considered statistically significant. BMI: Body mass index; HDL: High-density lipoprotein; TG: Triglycerides; SD: Standard deviation

Table 2. The mean value of global and segmental longitudinal left ventricular (LV) strain (ϵ_{LL}) in individuals with metabolic syndrome and control group

Variables		With metabolic syndrome (n = 36)	Without metabolic syndrome (n = 39)	P
Segmental ϵ_{LL} (%)	Anteroseptal			
	Apical	-19.22 ± 4.5	-24.38 ± 4.9	< 0.001
	Mid	-17.69 ± 2.5	-19.15 ± 3.2	0.037
	Base	-19.95 ± 2.9	-21.15 ± 3.3	0.106
	Anterolateral			
	Apical	-16.50 ± 4.7	-23.70 ± 3.1	< 0.001
	Mid	-16.90 ± 4.0	-20.10 ± 3.4	< 0.001
	Base	-17.50 ± 5.0	-18.30 ± 4.1	0.437
	Inferoseptal			
	Mid	-18.00 ± 3.1	-19.80 ± 2.2	0.006
	Base	-15.50 ± 3.5	-17.50 ± 2.5	0.006
	Inferolateral			
	Mid	-17.30 ± 4.4	-20.10 ± 3.5	0.004
	Base	-18.10 ± 6.3	-18.90 ± 4.1	0.526
	Anterior			
	Apical	-16.70 ± 5.7	-20.70 ± 3.9	< 0.001
	Mid	-16.70 ± 5.7	-20.70 ± 3.9	< 0.001
	Base	-16.00 ± 7.1	-19.00 ± 4.4	0.030
	Inferior			
	Apical	-19.70 ± 3.9	-25.10 ± 3.9	< 0.001
Mid	-19.80 ± 4.0	-21.60 ± 3.2	0.030	
Base	-18.40 ± 4.2	-20.50 ± 3.7	0.021	
Apical cap	-22.10 ± 3.1	-24.40 ± 2.2	0.002	
Global ϵ_{LL} (%)		-18.41 ± 2.2	-21.20 ± 2.1	< 0.001

The independent t-test was used for comparison of all variables between groups. $P < 0.050$ was considered statistically significant.

Considering the limitations of TDI-derived strain and the fact that more general conclusion can be drawn from studies on populations in whom metabolic syndrome is more prevalent, in a multi-ethnic study using STE which was superior to our study regarding its larger sample size, focus on both circumferential and longitudinal LV myocardial strain and also providing data on reproducibility of parameters, individuals with metabolic syndrome had lower circumferential and longitudinal myocardial shortening as indicated by less negative ϵ_{CC} and ϵ_{LL} than those without metabolic syndrome even after adjusting for age, ethnicity, LV mass and LVEF and it was significantly correlated with magnetic resonance imaging (MRI) findings.⁹

In addition to reduced values of global ϵ_{LL} , our study also depicted significantly reduced STE-derived segmental ϵ_{LL} in patients with metabolic syndrome except for basal anteroseptal, basal anterolateral and basal inferolateral segments which may be attributable to mid-wall ϵ_{LL} being inherently highest in the apex and lowest in the base¹⁶ contributing to less statistically significance of compared basal strains between two groups. ϵ_{LL} is an angle-independent parameter with the established prognostic value¹¹ for

which the same vendor and the same software were used for measurement in all examinations to eliminate the vendor- and software dependency of this valuable parameter.

Although this study is the only study assessing both global and segmental longitudinal STE-derived strain in subclinical metabolic syndrome, it has some limitations including use of ϵ_{LL} as the single STE-derived parameter due to lack of equipped modalities. In addition, most of the enrolled patients were middle-aged and therefore, the results cannot be generalized to extremes of age groups in adult population. These results would be confirmed by further similar studies worldwide enrolling increased number of subjects whose limited number is one of the other shortages of this study which curtail our ability to draw definitive conclusions for a screening program.

Conclusion

Based on our study, the STE-derived global longitudinal LV strain is reduced in asymptomatic patients with metabolic syndrome and LVEF $\geq 55\%$. Less value of longitudinal LV strain is also evident in most of LV myocardial segments. Consequently,

LV myocardial longitudinal strain assessed by STE is an early marker of LV systolic dysfunction in asymptomatic population with metabolic syndrome.

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Conflict of Interests

Authors have no conflict of interests.

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