**ABSTRACT**

**Objective:** Left ventricular (LV) systolic synchrony is defined as simultaneous activation of corresponding cardiac segments. Impaired synchrony has some adverse cardiovascular effects, such as LV dysfunction and impaired prognosis. Epicardial fat tissue (EFT) is visceral fat around the heart. Increased EFT thickness is associated with some disorders, such as LV dysfunction and hypertrophy, which play a role in the impairment of LV synchrony. However, the relationship between EFT and LV systolic synchrony has never been assessed. Thus, we aimed to evaluate the possible relationship between EFT and LV synchrony in this study.

**Methods:** The study population consisted of 55 consecutive patients (mean age 46.4±13.4 years, 32 female) without bundle branch block (BBB). EFT and LV systolic synchrony were evaluated by transthoracic echocardiography using 2D and tissue Doppler imaging. Maximal difference (Ts-6) and standard deviation (Ts-SD-6) of time to peak systolic (Ts) myocardial tissue velocity obtained from 6 LV basal segments were used to assess LV synchrony. Multiple regression analysis was used to detect the independently related factors to LV synchrony.

**Results:** The mean values of EFT thickness, Ts-6, and Ts-SD-6 were found to be 2.7±1.6 mm (ranging from 1-7 mm), 20.1±14.2 msec, and 7.7±5.6, respectively. EFT thickness also was independently associated with Ts-6 (β=0.332, p=0.01) and Ts-SD-6 (β=0.286, p=0.04).

**Conclusion:** EFT thickness is associated with LV systolic synchrony in patients without BBB. (Anatol J Cardiol 2015; 15: 990-4)

**Key words:** epicardial fat tissue, left ventricular synchrony, ventricular dyssynchrony

**Introduction**

Left ventricular (LV) synchrony refers to simultaneous and coordinated activation of certain ventricular segments. Impairment of LV systolic synchrony, known as dyssynchrony, may lead to reduced systolic function, myocardial perfusion, exercise capacity, prognosis, and quality of life (1-3). It has also been suggested that pacemaker-induced impaired synchrony may be related to the development of LV dysfunction in patients with normal ejection fraction (4), and impaired LV synchrony is an independent factor of deterioration of heart failure (5). However, factors affecting LV synchrony have not yet been understood thoroughly.

Epicardial fat tissue (EFT), which is a kind of visceral adipose tissue, has a close interaction with myocardium and coronary arteries (6, 7). EFT releases a variety of proinflammatory cytokines, such as interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α, which play important roles in the development of several cardiovascular disorders, such as atherosclerosis and atrial fibrillation (6-9). EFT thickness is also related to LV mass, atrial dimensions, and diastolic function (10, 11). These disorders are associated with impaired LV synchrony (12-15). However, to date, the relationship between EFT and LV synchrony has not been investigated. Hence, the purpose of this study was to evaluate this possible relationship.

**Methods**

**Patient selection**

Study had a prospective observational cross-sectional design. Seventy-five consecutive patients without bundle branch block (BBB) were enrolled age between 26 and 77 in study. Diseases that are obviously associated with impaired LV synchrony were defined as exclusion criteria which there were 15 patients, including presence of BBB, dilated or hypertrophic cardiomy-
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Echocardiographic examination

Assessment of M-mode and Doppler echocardiography

Transthoracic 2-dimensional (2D), Doppler, and tissue Doppler imaging (TDI) echocardiography were performed according to the recommendations of the American Society of Echocardiography (17) using a commercially available system (Vivid 7, GE Vingmed Ultrasound AS, Horten, Norway). Subjects were examined in the left lateral recumbent position using standard parasternal (short- and long-axis) and apical views (two-chamber, four-chamber, and long-axis). Systolic (LVESD) and diastolic (LVEDD) dimensions of the LV and left atrium (LA) diameter were measured by 2-dimensional guided M-mode echocardiography. LV function was assessed by ejection fraction using the modified biplane Simpson's rule. LV mass index (LVMI) was calculated using the Devereux formula (18). For LV diastolic filling patterns, Doppler sample volume was put into the middle of the LV inflow tract 1 cm below the plane of the mitral annulus in the apical four-chamber view. Transmitral filling velocities, including peak early (E) diastole, were obtained. To obtain optimal tissue velocities, the high-pass filter was bypassed, and gains were minimized. The Nyquist limit was adjusted to a velocity range of -15 cm/s to 15 cm/s. To optimize the spectral display of myocardial velocities, monitor sweep speed was increased to 50-100 mm/s. After getting the optimal images, early diastolic (e') tissue velocity from the lateral mitral annulus was obtained. Then, the E/Em ratio was calculated to be an indicator of diastolic function.

Assessment of LV synchrony and epicardial fat tissue

LV systolic synchrony was assessed by TDI by using the six-basal-segmental model (5, 19-21). Initially, the time to the onset of systolic (Ts) myocardial tissue velocity from the onset of QRS signal was measured for 6 LV basal segments, including septal, lateral, anterior, inferior, posterior, and anteroseptal. Then, 2 systolic synchrony indices were computed: maximal difference in Ts between any 2 of the 6 basal LV segments (Ts-6) and standard deviation of Ts of the 6 basal LV segments (Ts-SD-6).

EFT was evaluated by measurement of its thickness using 2D transthoracic echocardiography. EFT thickness was measured by a predefined method (7). According to this method, EFT was defined as echo-free space in front of the right ventricle free wall on transthoracic parasternal long-axis images (Fig. 1). The measurement of EFT thickness was made to be perpendicular to the aortic annulus at end-diastole. All measurements were performed for three consecutive cardiac cycles, and an average value was obtained.

Reproducibility

Echocardiographic images were digitally recorded and stored onto the device. Recorded data of 20 patients were evaluated by two independent cardiologists who were blinded the patients’ data. Then, intra- and interobserver variability was assessed by the method described by Bland-Altman for EFT, Ts-6, and Ts-SD-6 (22, 23). Intraobserver variability was computed as 4.4% for EFT, 3.7% for Ts-6, and 3.6% Ts-SD-6. Interobserver variability was calculated as 5.3% for EFT, 4.1% for Ts-6, and 4.6% for Ts-SD-6.

Statistical analysis

Continuous variables were described as both mean ± standard deviation (SD). Normal distributions of values were assessed by using the Kolmogorov-Smirnov test. Categorical variables were expressed as percentage values. Pearson’s and Spearman’s correlation coefficients were used to assess the relationship among the parameters when appropriate. Multiple regression analysis was used to identify factors independently associated with LV synchrony indices. A p value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS (SPSS, 13.0, Inc, Chicago, Illinois, USA).
Results

Demographic and echocardiographic features

Seventy-five consecutive patients were enrolled age between 26 and 77 in study. Twenty patients who had exclusion criteria were excluded from the study. Baseline demographic features and echocardiographic parameters of the study population are shown in Tables 1 and 2.

Relationship between EFT and other variables

EFT thickness was correlated with age (r=0.6, p<0.001), BMI (r=0.42, p=0.001), LA diameter (r=0.37, p=0.005), LVMI (r=0.49, p<0.001), and E/e’ ratio (r=0.38, p=0.004).

Relationship between LV synchrony indices and other variables

Correlation of Ts-6 and other variables

In the univariate correlation analysis, a significant correlation between Ts-6 and EFT thickness (r=0.447, p=0.001), LVEF (r=0.42, p=0.001), LVEDD (r=0.327, p=0.015), and LVMI (r=0.648, p<0.001) was found (Fig. 2). In the multivariable analysis, Ts-6 was independently associated with EFT thickness (beta=0.332, p=0.01), LVMI (beta=0.679, p<0.001), and LVEDD (-0.360, p=0.03) (Table 3).

Correlation of Ts-SD-6 and other variables

In the univariate correlation analysis, there was a significant relationship between Ts-SD-6 and EFT thickness (r=0.428, p=0.001), LVEF (r=0.426, p=0.001), LVEDD (r=0.364, p=0.007), and LVMI (r=0.676, p<0.001) (Fig. 3). There was also an independent relationship between Ts-SD-6 and EFT thickness (beta=0.286, p=0.04) and LVMI (beta=0.704, p<0.001) (Table 3).

Discussion

In this study, we found that both Ts-6 and Ts-SD-6 were correlated with LV systolic and diastolic diameter, LVMI, and EFT thickness. In addition, EFT thickness and LVMI were independently associated with Ts-6 and Ts-SD-6.

Impaired LV synchrony has recently been the subject of interest, because it may cause a lot of cardiovascular disorders, such as myocardial perfusion, exercise capacity, prognosis, and quality of life (1-3). In addition, adverse effects of impaired LV synchrony on systolic and diastolic function indi-
Table 3. Multiple regression analysis between synchronicity indices and other variables

| Ts-6 | 95% CI |
|------|--------|
| β    | B      | Lower | Upper | P     |
| Age  | -0.262 | -0.277| -0.575| 0.21  | 0.67  |
| LVEDD| 0.303  | 0.110 | 2.330  | 0.07  |
| LVESS | -0.360 | -1.311| -2.525 | -0.097| 0.03  |
| LVMI | 0.679  | 0.421 | 0.239  | 0.602 | <0.001|
| EFT thickness | 0.332 | 2.945 | 0.680 | 5.211 | 0.01  |

| Ts-SD-6 | 95% CI |
|---------|--------|
| β      | B      | Lower | Upper | P     |
| Age    | -0.265 | -0.115| -0.239| 0.010 | 0.07  |
| LVEDD  | 0.241  | 0.246 | -0.162| 0.853 | 0.18  |
| LVESS | -0.282 | -0.407| -0.919| 0.104 | 0.12  |
| LVMI   | 0.704  | 0.171 | 0.098  | 0.244 | <0.001|
| EFT thickness | 0.286 | 0.933 | 0.050 | 1.937 | 0.04  |

EFT - epicardial fat tissue; LVEDD - left ventricular end-diastolic diameter; LVESD - left ventricular mass index; LVMI - left ventricular mass index. Constant values: 16.311 for Ts-6 and 3.978 for Ts-SD-6. Multiple linear regression analysis.

Our study had some limitations. First, our study population had a relatively small number of patients. Second, coronary ischemia, which may lead to dyssynchrony, was not specifically assessed by coronary angiography or myocardial scintigraphy in the study. However, if there was any suspicion of clinically important coronary artery disease, including anginal symptoms, abnormal ischemic ECG findings, and myocardial wall motion abnormalities by echocardiography, patients were assessed by exercise testing. Patients with a positive result for exercise testing were excluded from the study. Third, the blood level of inflammatory cytokines was not obtained. Fourth, this study had a cross-sectional observational design, which may not provide information on the clinical significance and longitudinal effects of our findings. Therefore, our study results should be confirmed by a further study.

Conclusion

EFT thickness is associated with LV systolic synchrony indices. EFT may play a role in the impairment of LV synchrony.

Conflict of interest: None declared.

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