Relationship between epicardial fat tissue and left ventricular synchronicity: An observational study

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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 crossectional 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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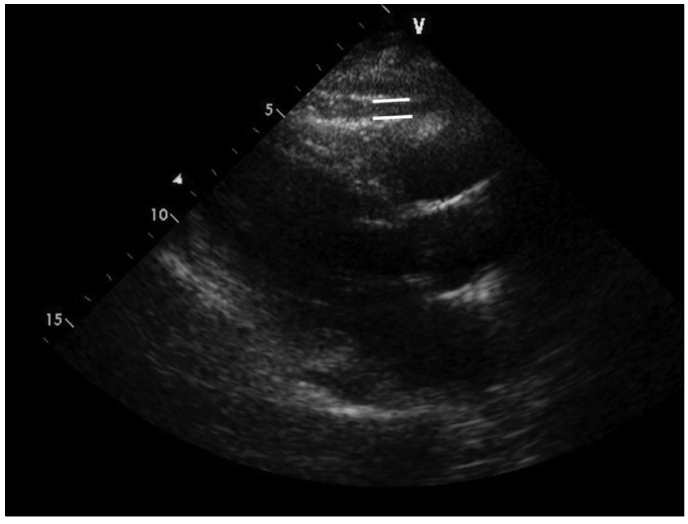

Figure 1. Transthoracic 2-dimensional echocardiography showing epicardial fat tissue as an echo-free space in front of the right ventricle free wall

opathy, known coronary artery disease (angina pectoris, history of myocardial infarction, percutaneous coronary intervention, and coronary bypass), heart failure (EF <50%), valvular heart disease (except for the mild form), valve replacement, atrial fibrillation, uncontrolled hypertension (blood pressure >140/90 mm Hg), uncontrolled diabetes mellitus (random blood glucose >198 mg/dL) (16), and poor echocardiographic imaging. Full demographic data, biochemical blood tests, and electrocardiography (ECG) were obtained from the entire study population. The presence of blood pressure >140/90 mm Hg or the use of antihypertensive medication was defined as hypertension. Body mass index was calculated as weight (kilograms) divided by the square of height (meters squared). Exercise testing was given if there was a suspicion of clinically significant coronary artery disease in the history, electrocardiography, or echocardiography. Five patients with positive exercise testing were excluded from the study. The study protocol was approved by the institutional Ethics Committee (approval date 14.05.2013, approval no: 17522305/326).

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).

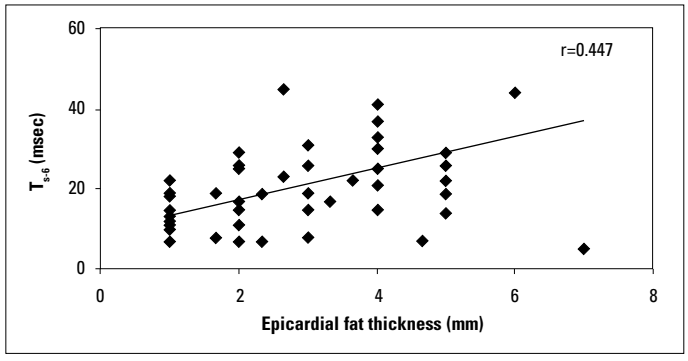

Figure 2. Relationship between epicardial fat tissue thickness and Ts-6 by correlation analysis

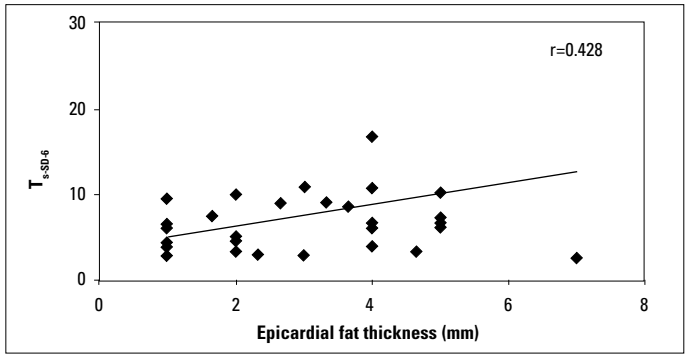

Figure 3. Relationship between epicardial fat tissue thickness and Ts-SD-6 by correlation analysis

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), LVESD (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), LVESD (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).

Table 1. Baseline demographic properties of the study population

	n (%)	mean±SD
Age, years		46.4±13.4
BMI, mean kg/m^2		27.4±5.1
Fasting blood glucose, mg/dL		100.7±25.9
Creatinine, mg/dL		0.8±0.18
QRS duration, ms		88±12.6
Heart rate, beats/min		72.5±13.9
Gender, female	32 (58.2%)	
Hypertension	10 (18.2%)	
Diabetes mellitus	5 (9.1%)	
Smoking	4 (7.3%)	

BMI - body mass index; BP - blood pressure; SD - standard deviation

Table 2. Echocardiographic parameters of the study population

	Mean±SD
EFT thickness, mm	2.7±1.6
LVESD, mm	30.4±3.9
LVEDD, mm	48.1±3.9
Ejection fraction, %	64.5±5.6
LA, mm	34.7±4.6
IVS, mm	10±1.7
PW, mm	9.6±1.5
LVMI, gr/m^2	90.5±22.8
E/e'	7.3±3.2
Ts-6, msec	20.1±14.2
Ts-SD-6	7.7±5.6

E - early transmitral filling peak velocity; e' - early diastolic mitral annular tissue velocity; EFT - epicardial fat tissue; IVS - interventricular septum; LA - left atrium; LVEDD - left ventricular end-diastolic diameter; LVESD - left ventricular end-systolic diameter; LVMI - left ventricular mass index; PW - posterior wall; Ts - time to peak systolic myocardial velocity; Ts-6 - maximal difference in Ts between any 2 of the 6 basal LV segments; Ts-SD-6 - standard deviation of Ts of the 6 basal LV segments

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
LVESD	0.303	1.110	-0.110	2.330	0.07
LVEDD	-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
LVESD	0.241	0.346	-0.162	0.853	0.18
LVEDD	-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	0.993	0.050	1.937	0.04

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

ces were reported in different patient populations (24-26). However, to date, the determinants of impaired LV synchrony have not been figured out.

EFT is true visceral fat and has a close relationship with the myocardium and coronary arteries (6, 7). For example, EFT acts as an immediate energy source for myocardium that releases free fatty acids and is protective for myocytes from exposure to excessive free fatty acids (27, 28). EFT also plays an important role in the inflammatory process in the cardiovascular system because, it releases several bioactive molecules, including adiponectin and proinflammatory cytokines (6-9). In addition, in the last decade, many studies suggested that EFT was associated with several adverse cardiovascular effects, including atherosclerosis (29).

In this study, we found an independent relationship between EFT thickness and LV synchrony indices. The interaction between EFT and the myocardium can be proposed to explain this relationship, because EFT is associated with both structural and ultrastructural myocardial changes, including myocardial fibrosis. Iacobellis et al. (10, 11) also reported that EFT was associated with LV mass, atrial dimensions, and diastolic function. They also considered that both the direct effects and biochemical features of adipose tissue, including insulin resistance, high free fatty acids levels, B-adrenergic activity, and inflammation, may explain these findings. Actually, EFT is associated with both local and systemic inflammation, and it releases several bioactive inflammatory cytokines, including IL-1, IL-6, and TNF-α (6-9, 30). These inflammatory cytokines play an important role in myocardial remodeling. In our study, we found a significant relationship between EFT thickness and LVMI, LA diameter, and E/e' ratio, consistent with Iacobellis's study. Therefore, we considered that EFT might be related with ultrastructural myocardial changes and interstitial fibrosis in our study. This ultrastructural remodeling may also alter intercellular electrical coupling and intracellular calcium handling, which leads to the impairment of coordination between regions of the ventricle, resulting in LV dyssynchrony.

Study limitations

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.

Peer-review: Partially external peer-reviewed.

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