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ORIGINAL ARTICLE

Atrial Electromechanical Properties in Coeliac Disease

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Background Coeliac disease (CD) is an autoimmune and inflammatory disorder of the small intestine. There is reasonable evidence linking inflammation to the initiation and continuation of atrial fibrillation (AF) in inflammatory conditions. Atrial electro-mechanic delay (EMD) was suggested as an early marker of AF in previous studies. The objectives of this study were to evaluate atrial electromechanical properties measured by tissue Doppler imaging and simultaneous electrocardiography (ECG) tracing in patients with CD.

Methods Thirty-nine patients with coeliac disease (CD), and 26 healthy volunteers, matched for age and sex, were enrolled in the study. Atrial electromechanical properties were measured by using transthoracic echocardiography and surface ECG. Interatrial electro-mechanic delay (EMD), left intraatrial EMD, right intratrial EMD were calculated.

Results There was no difference between CD patients and healthy volunteers in terms of basal characteristics. Patients with CD had significantly prolonged left and right intraatrial EMDs, and interatrial EMD compared to healthy controls ($p= 0.03$, $p= 0.02$, $p<0.0001$, respectively). Interatrial EMD was positively correlated with age, disease duration, anti-gliadin IgG, anti-endomysium and disease status. In multiple linear regression, interatrial EMD was independently associated with disease duration, anti-endomysium and disease status after adjusting for age and sex.

Conclusions In the present study, atrial EMDs were found significantly higher in patients with CD compared with healthy individuals. Measurement of atrial EMD parameters might be used to predict the risk of development of AF in patients with CD.

Keywords Coeliac disease • Atrial fibrillation • Atrial electromechanical delay

Introduction

Coeliac disease (CD), also known as gluten intolerance, is an autoimmune disorder of the small intestine that occurs in predisposed individuals. Small intestinal mucosal inflammation and injury occur after ingestion of wheat gluten or related rye and barley proteins. Small intestinal villous atrophy and crypt hyperplasia are dominant pathological findings in paediatric cases; however, lymphocytic infiltration is more common in the adult form of the disease with or without the aforementioned signs [1,2].

There are some evidences from earlier studies about the association between the CD and cardiovascular diseases. Ludvigsson et al. have shown that the incidence of ischaemic

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heart disease increases in individuals with CD or small intestinal inflammation [3]. Sari et al. have found endothelial dysfunction associated with flow mediated dilatation, which is a subclinical sign of atherosclerosis in patients with CD [4]. An association between CD and idiopathic dilated cardiomyopathy has been suggested in some studies [5,6]. Atrial fibrillation, a common cardiac arrhythmia, is a kind of supraventricular tachyarrhythmia, associated with substantial morbidity and mortality. Its prevalence increases with advancing age. Atrial fibrillation is associated with a five-fold increased risk of stroke and two-fold increased risk of mortality [7]. Systemic inflammation plays a significant role in AF pathogenesis and AF risk factors have been found to be linked to oxidative stress [8,9]. Inflammation and oxidative stress have been found to be responsible molecular mechanisms of CD [10]. There are two studies that establish association between CD and AF. First is West et al., which revealed that individuals with CD are slightly more likely to have had AF [odds ratio: 1.26 (95% confidence interval: 0.97–1.64)] [11]. Second is a national cohort study done by Emilsson et al., which indicated that CD, verified by intestinal biopsy, poses an increased risk of AF [odds ratio:1.45, 95% confidence interval: 1.31–1.62] [12].

Some non-invasive electrocardiographic and combined electro-echocardiographic methods have been defined to predict the development of AF. The atrial electro-mechanic delay (EMD) is associated with increased frequency and susceptibility of atrial fibrillation. Atrial electromechanical properties by using conventional and tissue Doppler echocardiography and electrocardiography have not been assessed earlier in patients having CD. In this study, we aimed to investigate the relation between atrial electromechanical properties in patients with CD.

Subjects and Methods

The study was conducted between September 2014 and January 2015, 53 patients were assessed with a previous diagnosis of biopsy proven coeliac disease from gastroenterology outpatients and 14 of them were excluded. The remaining 39 patients and 26 healthy subjects, prospectively matched for age and sex, from the outpatient clinic of cardiology and gastroenterology were enrolled in the study. At the time of the recruitment all patients were on a gluten free diet for at least the previous three months. Patients with one or more of the following features were excluded: autoimmune disorders; valvular, structural, coronary, congenital heart disease; rhythm disorders; active infection; pregnancy; diabetes mellitus; hypertension; thyroid diseases; chronic obstructive pulmonary disease; abnormal serum electrolyte values; chronic systemic disease; renal failure and dietary incompliance in terms of gluten were excluded. Patients who were diagnosed with coeliac disease less than one year were also excluded. None of the patients were under treatment with corticosteroids, immunosuppressants and antiarrhythmics. The study protocol was approved by the local ethics committee and an informed consent was obtained from each subject before the study enrolment.

The biochemical tests included the lipid profile: total cholesterol, low density lipoprotein, high density lipoprotein, total triglyceride levels, fasting glucose level, iron, total iron-binding capacity, liver and renal function tests. In addition, haemogram, thyroid function tests, ferritin, vitamin B12, folic acid were also measured. The weight and height of the participants were measured, and their BMIs (kg/m^2) were calculated. These tests were performed at the biochemistry laboratory of Diskapi Training and Research Hospital. Echocardiographic examination and evaluation of patients were performed with Philips iE33 echocardiographic imaging system (Andover, MA, USA) with a 2.5-5 MHz transducer. Examinations were performed by a single experienced cardiologist who was blind to the patients and their characteristics.

The patients were evaluated in the left lateral decubitus position after measuring their blood pressure. A continuous one-lead ECG was obtained during all the examinations. The average of three consecutive beats was used to calculate the associated parameters. The basic echocardiographic parameters, such as left atrium dimension, LV end-systolic and end-diastolic dimensions, diastolic ventricular septal thickness, and diastolic LV posterior wall thickness, were measured in the parasternal long-axis view. Left ventricular EF was estimated using the Simpson's rule.

Electromechanical properties of the atria were determined by tissue Doppler imaging. Before the study, the Nyquist limit was adjusted to 15-20 cm/sec and the monitor sweep speed was set to 50-100 mm/sec to optimise the spectral display of myocardial velocities. The pulsed Doppler (PW) sample volume was placed at the LV lateral and septal mitral annulus, subsequently at the septal mitral annulus and right ventricular tricuspid annulus in apical four-chamber view. Myocardial systolic (S), early diastolic (E), and atrial systolic (A) waves were measured by PW Doppler; and E/E′ ratio was calculated. Atrial electro-mechanic coupling was considered from the onset of P wave on ECG to the beginning of A wave in tissue Doppler (PA), is illustrated in Figure 1. PA interval was measured from the lateral mitral annulus; septal mitral annulus and right ventricular tricuspid annulus were called PA lateral, PA septum, PA tricuspid, respectively [13]. The difference between the lateral and tricuspid PA intervals was defined as interatrial EMD; the difference between the septal and tricuspid PA intervals was defined as right intraatrial EMD; the difference between the lateral and septal PA intervals was defined as left intraatrial EMD.

Reproducibility

Fifteen subjects were selected randomly from the patients for assessing intraobserver variability. Measurements were repeated under the same basal conditions. Reproducibility of atrial electromechanical coupling obtained by TDI was assessed by coefficient of variation between measurements. Intraobserver variability was 5.9% for lateral, 5.5% for PA septum, and 6.3% for PA tricuspid, respectively.