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Association between aortic stiffness and left ventricular function in inflammatory bowel disease

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Abstract

Background: *Recent studies have reported an increased incidence of both aortic aortic stiffness and left ventricular (LV) systolic and diastolic dysfunction in patients with inflammatory bowel disease (IBD). However, the association between aortic stiffness and the LV function has not been fully defined. We aimed to investigate the relationship between aortic stiffness and the LV function in IBD patients.*

Methods and Results: *Seventy-two patients with IBD (56 cases of ulcerative colitis and 16 cases of Crohn's disease) and 50 healthy controls were consecutively enrolled in this study. The LV systolic and diastolic functions were assessed using conventional echocardiographic techniques, including tissue Doppler echocardiography. The degree of aortic strain and distensibility were calculated based on the aortic diameters measured on M-mode echocardiography at the level of 3 cm above the aortic valve and the blood pressure values obtained on sphygmomanometry. There were significant differences between the IBD and control group in the degree of aortic strain and distensibility. Significant differences were also observed between the patient and control groups in the parameters of the LV systolic and diastolic functions. Moreover, aortic stiffness was found to be associated with the LV function in the patient group.*

Conclusions: *There is a significant relationship between aortic stiffness and LV systolic and diastolic dysfunction in patients with IBD, based on the findings of this study. The parameters of aortic elasticity measured according to 2-dimensional echocardiographic methods can be beneficial for predicting early cardiovascular risk in cases of IBD.* (Cardiol J 2016; 23, 2: 202–210)

Key words: aortic stiffness, left ventricular function, inflammatory bowel disease, tissue Doppler echocardiography

Introduction

Inflammatory bowel disease (IBD), which is commonly diagnosed in young adults, is composed of a group of inflammatory diseases of the colon and small intestine occurring in genetically predisposed individuals. Ulcerative colitis (UC) and Crohn's disease (CD) represent the two major forms of IBD, both of which have a chronic course and are characterized by episodes of remission and exacerbation. Recent studies have reported that, despite the fact that the prevalence of traditional cardiovascular (CV) risk factors is lower than in the general population [1–3], the risk of CV events is increased in IBD

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patients [4, 5], suggesting that additional mechanisms, such as inflammation, could be responsible for the excess CV risk observed in IBD cases. In these subjects, the low CV risk associated with the low prevalence of traditional CV risk factors may be at least partly counterbalanced by the increased CV risk associated with chronic inflammation. In cases of IBD, inflammation and atherosclerosis are closely linked. Inflammation mediates its effects on atherosclerosis via both modulating traditional risk factors and directly affecting the vessel wall [6].

In a recent small study, it was shown that arterial stiffness is increased in IBD patients [7]. The role of arterial stiffness in the development of CV diseases is well known [8]. In particular, the presence of arterial stiffness in large arteries, such as the aorta, has been reported to be the best predictor of CV morbidity and mortality [9]. Although there are several parameters used in assessments of arterial stiffness, the degree of stiffness can be evaluated with echocardiography using relatively simple, non-invasive methods. Both aortic distensibility (AD) and aortic strain (ASt) are elasticity indices for the aorta and reflect the degree of aortic stenosis (AS) [8, 10]. While AS is known to be related to atherosclerosis, its association with cardiac systolic and diastolic functions in cases of IBD has not been fully evaluated. In this study, we aimed to evaluate the association of AS with the left ventricular (LV) systolic and diastolic functions in patients with IBD.

Methods

Study patients and protocol

A total of 72 patients with IBD (56 patients with UC and 16 patients with CD, ages 18–50 years) and 50 matched healthy controls treated between December 2013 and October 2014 were consecutively enrolled into this prospective study. The diagnosis of IBD was confirmed using established criteria consisting of clinical, radiological, endoscopic and histological findings. The medical history of each patient, including the disease duration and medications, was collected, and a routine physical examination was conducted. Patients with an age over 50 or under 18 years, structural heart disease, overt CV disease based on the presence of abnormal echocardiographic findings, complaints related to peripheral or coronary artery disease and a history of cerebrovascular disease, hypertension (HT) as defined by a blood pressure (BP) of at least 140/90 mm Hg and/or the use of anti-hypertensive medications, hyperlipidemia and/or the use of lipid-lowering medications, diabetes mellitus (DM) and/or the use of anti-diabetic medications, pulmonary disease or neoplastic or chronic systemic diseases were excluded from this study. All subjects were informed about the study protocol, and written informed consent was obtained from each volunteer. Approval for the study protocol was obtained from the local Ethics Board.

Echocardiography

Conventional echocardiographic measurements. The echocardiographic evaluations of all subjects were performed by a single, experienced cardiologist who was not informed of the clinical or laboratory findings of the patients. The echocardiographic examinations were carried out using a 2.5- to 3.5-MHz transducer with the Vingmed System 7 (Vivid 7, GE, Horten, Norway). M-mode echocardiography and a quantitative analysis were conducted using parasternal long axis images based on data provided by the American Society of Echocardiography [11]. The LV systolic and diastolic functions were analyzed using standard two-dimensional (2D) echocardiography, M-mode echocardiography, pulsed-wave (PW) echocardiography and tissue Doppler echocardiography (TDE). The LV end-diastolic diameter (LVEDD) and LV end-systolic diameter (LVESD), left atrium (LA) diameter, interventricular septum (IVS) and posterior wall thicknesses were obtained using M-mode echocardiographic tracings under the guide of 2D imaging. The left ventricular ejection fraction (LVEF) was calculated according to the biplane modified Simpson method. The mitral inflow early diastolic wave (E), late diastolic wave (A), E/A ratio, deceleration time (DT), isovolumetric contraction time (IVCT), ejection time (ET) and isovolumetric relaxation time (IVRT) were measured on PW echocardiography, and the myocardial performance index (MPI) was calculated by dividing the sum of IVRT and IVCT by ET.

Tissue Doppler imaging

The myocardial systolic wave (S'), early diastolic myocardial wave (E'), late diastolic myocardial wave (A'), E'/A' ratio, myocardial IVCT (IVCTm), myocardial ET (ETm), IVCTm/ETm ratio and myocardial IVRT (IVRTm) were measured on color TDE conducted on respectively lateral parts of the mitral annulus. MPI was calculated by dividing the sum of IVCTm and IVRTm by the ETm value. The E/E' ratio was measured by dividing the mitral inflow early diastolic wave (E) by the early diastolic myocardial wave (E').

Measurement of aortic stiffness

The diameter of the ascending aorta was measured from the same view on the M-mode tracing at a level 3 cm above the aortic valve. The systolic aortic diameter (AoSD) was measured at the maximal anterior motion of the aorta, whereas the diastolic aortic diameter (AoDD) was measured at the peak of the QRS complex on the simultaneously recorded electrocardiogram. The systolic BP (SBP) and diastolic BP (DBP) values were measured on both arms using an external sphygmomanometer, and the higher value was recorded. The pulse pressure (PP) was calculated as SBP minus DBP. The degree of ASt (%) was calculated as (AoSD – AoDD)/AoDD, and AD (10^{-6} cm^2 × dyn^{-1}) was calculated as (2 × ASt)/PP.

Statistical analysis

The data analysis was performed using the SPSS 17 software package (Statistical Package for Social Sciences Inc., Chicago, IL, USA). The normality of the distribution of continuous variables was analyzed using the Shapiro-Wilk test. Descriptive statistics are expressed as the mean ± standard deviation or median (minimum–maximum) for continuous variables and as the number of observations and percentages (%) for categorical variables. The significance of the differences in the measurements obtained for the control and patient groups was analyzed using Student's t-test or the Mann-Whitney U test. We used ANOVA and a post hoc analysis for multiple comparisons between the control group, IBD group, UC group and CD group. The Pearson χ^2 test was used to compare categorical variables. A Pearson's analysis was used to calculate the correlation coefficient. A p value of < 0.05 was considered to be statistically significant.

Results

Demographic characteristics of the subjects

The characteristics of the study populations are presented in Table 1. The IBD patients were relatively young (mean age: 41.6 ± 11.7 years) and predominantly male (46 [63%] men and 26 [37%] women). Among the IBD patients, 78% (n = 56) had UC and 22% (n = 16) had CD. All IBD patients were in remission. The mean disease duration was 68.2 ± 18.7 months (minimum to maximum: 1–240 months). Of the IBD patients, 84% (n = 60) were

Table 1. The demographic characteristics of the subjects in the study groups.

Variables	IBD group (n = 72)	Control group (n = 50)	P
Age [years]	41.6 ± 11.7	39.9 ± 7.9	0.358
Gender (male/female)	46/26	29/21	0.515
Body mass index [kg/m^2]	27.6 ± 4.5	27.0 ± 3.5	0.429
Systolic BP [mm Hg]	121.3 ± 12.2	118.7 ± 11.4	0.235
Diastolic BP [mm Hg]	74.6 ± 8.5	73.7 ± 8.1	0.551
Pulse [bpm]	76.8 ± 11.5	78.8 ± 10.6	0.341
Smokers [%]	13.9	20	0.374
Fasting blood glucose [mg/dL]	93.2 ± 9.9	95.4 ± 11.1	0.265
Total cholesterol [mg/dL]	173.6 ± 41.1	186.0 ± 37.7	0.093
LDL cholesterol [mg/dL]	102.4 ± 32.5	117.7 ± 30.2	0.010
HDL cholesterol [mg/dL]	47.3 ± 17.3	46.2 ± 9.5	0.681
Triglyceride [mg/dL]	117.1 ± 66.1	124.8 ± 69.7	0.537
Sedimentation [mm/h]	20.0 ± 20.9	11.8 ± 5.2	0.008
C-reactive protein [mg/L]	0.79 ± 1.7	0.54 ± 0.41	0.337
LVEDD [mm]	44.4 ± 3.4	44.5 ± 3.1	0.865
LVESD [mm]	26.5 ± 2.9	25.5 ± 2.7	0.074
Left atrium diameter [mm]	33.8 ± 3.8	33.7 ± 4.2	0.876
Interventricular septum [mm]	9.2 ±1.2	9.0 ± 1.0	0.281
Posterior wall [mm]	9.2 ± 1.1	8.8 ± 1.0	0.103
Left ventricular ejection fraction [%]	65.1 ± 0.1	65.3 ± 3.9	0.517

IBD — inflammatory bowel disease; BP — blood pressure; LDL — low-density lipoprotein; HDL — high-density lipoprotein, LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter

Table 2. Pulse-wave echocardiographic measurements of the study groups.

Variables	Controls (n = 50)	Total IBD patients (n = 72)	UC patients (n = 56)	CD patients (n = 16)
Early diastolic wave (E) [m/s]	0.90 ± 0.14	0.66 ± 0.16 (p < 0.001)	0.65 ± 0.17 (p < 0.001)	0.70 ± 0.16 (p < 0.001)
Late diastolic wave (A) [m/s]	0.74 ± 0.10	0.79 ± 0.19 (p = 0.072)	0.79 ± 0.19 (p = 0.093)	0.80 ± 0.20 (p = 0.097)
E/A ratio	1.23 ± 0.20	0.90 ± 0.34 (p < 0.001)	0.90 ± 0.35 (p < 0.001)	0.92 ± 0.28 (p < 0.001)
E/E′ ratio	0.06 ± 0.01	0.09 ± 0.02 (p = 0.001)	0.09 ± 0.02 (p < 0.001)	0.09 ± 0.02 (p < 0.001)
Deceleration time [ms]	168 ± 28	216 ± 42 (p < 0.001)	218 ± 41 (p < 0.001)	210.2 ± 44.4 (p < 0.001)
IVCT [ms]	69.7 ± 11.8	64.8 ± 13.4 (p = 0.042)	65.3 ± 13.7 (p = 0.083)	63.2 ± 12.4 (p = 0.066)
Ejection time [ms]	286.2 ± 29.8	286.3 ± 27.5 (p = 0.984)	287.3 ± 27.3 (p = 0.854)	282.5 ± 29.2 (p = 0.688)
IVRT [ms]	70.0 ± 13.8	86.3 ± 22.3 (p < 0.001)	87.1 ± 22.9 (p < 0.001)	83.6 ± 20.9 (p = 0.004)
Myocardial performance index	0.49 ± 0.08	0.53 ± 0.12 (p = 0.070)	0.53 ± 0.12 (p = 0.056)	0.51 ± 0.12 (p = 0.425)

IBD — inflammatory bowel disease; UC — ulcerative colitis; CD — Crohn's disease; IVCT — isovolumetric contraction time; IVRT — isovolumetric relaxation time

treated with salicylates only, whereas the remaining 16% (n = 12) were treated with salicylates and steroids or immunosuppressors. The healthy controls were well matched, and there were no significant differences between the IBD patients and healthy controls with respect to age, gender, body mass index (BMI), SBP, DBP, heart rate or the total cholesterol, plasma triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and C-reactive protein (CRP) levels. However, the low-density lipoprotein cholesterol (LDL-C) levels were significantly higher in the controls than in the IBD group (117.7 ± 30.2 vs. 102.4 ± 32.5 mg/dL, respectively, p = 0.010). The erythrocyte sedimentation rate was also significantly higher in the IBD group than in the controls (20.0 ± ± 20.9 vs. 11.8 ± 5.2 mm/h, p = 0.008).

Echocardiography

No statistically significant differences were detected between the patient and control groups with respect to the LVEDD, LVESD, LA diameter, IVS and posterior wall thicknesses and LVEF.

The PW echocardiographic measurements in the study groups are demonstrated in Table 2. Accordingly, the IVRT and DT values were significantly longer and the E waves, E/A ratio and IVCT values were significantly lower in the patient group; however, there were no statistically significant differences in the other parameters. A subgroup analysis of these parameters showed the same results for the UC and CD groups vs. the controls, except for IVCT, which, although lower than that seen in the controls, did not reach statistical significance in either the UC or CD groups. The PW TDE measurements of the septal wall in both groups are presented in Table 3. According to these results, the S', E', A' and E'/ A' values were significantly lower, while the IVRTm, IVCTm and MPI values were significantly higher in the patients group than in the controls. In addition to these findings, the E/E' ratio, a well-validated parameter of the diastolic function was found to be significantly higher in the patients with IBD than in the controls. Although mostly similar findings were observed in the subgroup analysis of the UC and the CD groups, the rise in the E'/A' ratio was not statistically significant (p = 0.079) in the CD group versus the controls.

Indices of aortic stiffness

The aortic elastic parameters are shown in Table 4. The degree of ASt (7.38 ± 2.6 vs. 15.1 ± ± 4.5; respectively, p < 0.001) and AD (3.3 ± ± 1.4 vs. 6.9 ± 2.2; respectively, p < 0.001) were found to be significantly lower in the IBD group than in the control group. Meanwhile, the AoDD (28.7 ± 3.8 vs. 2.66 ± 2.6 mm, respectively, p < 0.001) values were significantly higher in the

Table 3. Pulse-wave tissue Doppler echocardiography measurements of the septal wall.

Variables	Controls (n = 50)	Total IBD patients (n = 72)	UC patients (n = 56)	CD patients (n = 16)
Systolic myocardial wave (S') [cm/s]	10.6 ± 2.3	8.0 ± 1.4 (p < 0.001)	8.0 ± 1.5 (p < 0.001)	8.0 ± 1.3 (p < 0.001)
Early diastolic myocardial wave (E') [cm/s]	14.6 ± 3.3	8.2 ± 2.5 (p < 0.001)	7.8 ± 2.4 (p < 0.001)	9.4 ± 2.4 (p < 0.001)
Late diastolic myocardial wave (A') [cm/s]	10.4 ± 2.4	8.8 ± 1.6 (p < 0.001)	8.9 ± 1.6 (p < 0.001)	8.4 ± 1.9 (p = 0.006)
E'/A' ratio	1.4 ± 0.4	1.0 ± 0.4 (p < 0.001)	0.9 ± 0.4 (p < 0.001)	1.2 ± 0.55 (p = 0.079)
Myocardial isovolumetric contraction time [ms]	68.0 ± 13.2	78.2 ± 18.3 (p = 0.001)	78.5 ± 18.7 (p = 0.001)	77.1 ± 17.5 (p = 0.031)
Ejection time [ms]	291.1 ± 26.0	268.6 ± 19.9 (p < 0.001)	268.5 ± 17.4 (p < 0.001)	269.1 ± 27.6 (p = 0.005)
Myocardial isovolumetric relaxation time [ms]	65.3 ± 10.6	85.5 ± 15.8 (p < 0.001)	85.8 ± 15.4 (p < 0.001)	84.6 ± 17.6 (p < 0.001)
Myocardial performance index	0.45 ± 0.06	0.61 ± 0.12 (p < 0.001)	0.61 ± 0.12 (p < 0.001)	0.6 ± 0.14 (p < 0.001)

IBD — inflammatory bowel disease; UC — ulcerative colitis; CD — Crohn's disease

Table 4. Echocardiographic parameters of aortic elasticity in the study groups.

Variables	Controls (n = 50)	Total IBD patients (n = 72)	UC patients (n = 56)	CD patients (n = 16)
Aortic systolic diameter [mm]	30.5 ± 2.7	30.8 ± 3.8 (p = 0.709)	30.7 ± 3.0 (p = 0.804)	31.1 ± 4.8 (p = 0.591)
Aortic diastolic diameter [mm]	26.6 ± 2.6	28.7 ± 3.8 (p = 0.001)	28.6 ± 3.4 (p = 0.001)	29.0 ± 5.0 (p = 0.013)
Aortic strain [%]	15.1 ± 4.5	7.38 ± 2.6 (p < 0.001)	7.4 ± 2.7 (p < 0.001)	7.2 ± 2.4 (p < 0.001)
Aortic distensibility [10^{-3} $cm^2 \times dyn^{-1}$]	6.9 ± 2.2	3.3 ± 1.4 (p < 0.001)	3.4 ± 1.5 (p < 0.001)	3.1 ± 1.2 (p < 0.001)

IBD — inflammatory bowel disease; UC — ulcerative colitis; CD — Crohn's disease

IBD group, although there were no significant differences with respect to the AoSD values between the groups (p = 0.709). A subgroup analysis of the aortic elasticity parameters between the UC and CD groups and the controls also showed the same results as those observed in the IBD group and controls.

Echocardiographic correlates of aortic stiffness

The correlations between the echocardiographic measurements on LV tissue Doppler and the aortic elasticity parameters are shown in Tables 5 and 6. There were positive correlations between AD and S' (r= 0.40, p< 0.001), E' (r = 0.48, p < 0.001) and E'/A' ratio (r = 0.26, p = 0.003) and negative correlations between ASt and IVRTm (r = –0.43, p < 0.001), the E/E' ratio (r = –0.37, p < 0.001) and MPI (r = –0.44, p < 0.001). In addition, there were positive correlations between ASt and S' (r = 0.36, p = 0.001), E' (r = 0.53, p < < 0.001) and E'/A' (r = 0.30, p = 0.001) and negative correlations between ASt and IVRTm (r = –0.50, p < 0.001), E/E' (r = –0.38, p < 0.001) and MPI (r = –0.56, p < 0.001). The subgroup analysis showed similar findings between the UC and CD groups with respect to the ASt and LV TDE parameters, with the exception of an insignificant correlation between AD and E'/A' in the CD group (Table 5). In addition, there were insignificant correlations between ASt and S', A' and the E'/A' ratio in the CD group (Table 6).

Table 5. Correlation between aortic distensibility and left ventricular tissue Doppler echocardiographic parameters.

Variables	Co-efficient (p value)		
	Total IBD patients (n = 72)	UC patients (n = 56)	CD patients (n = 16)
Systolic myocardial wave (S′)	0.402 (< 0.001)	0.394 (< 0.001)	0.277 (0.024)
Early diastolic myocardial wave (E′)	0.488 (< 0.001)	0.474 (< 0.001)	0.350 (0.004)
Late diastolic myocardial wave (A′)	0.292 (0.001)	0.302 (0.002)	0.246 (0.046)
E/E′	–0.371 (< 0.001)	–0.361 (< 0.001)	–0.335 (0.006)
E′/A′	0.265 (0.003)	0.273 (0.005)	0.124 (0.321)
Myocardial isovolumetric contraction time	–0.260 (0.004)	–0.251 (0.010)	–0.227 (0.067)
Ejection time	0.271 (0.003)	0.262 (0.007)	0.204 (0.101)
Myocardial isovolumetric relaxation time	–0.431 (< 0.003)	–0.400 (< 0.001)	–0.418 (< 0.001)
Myocardial performance index	–0.444 (< 0.001)	–0.419 (< 0.001)	–0.439 (< 0.001)

IBD — inflammatory bowel disease; UC — ulcerative colitis; CD — Crohn's disease

Table 6. Correlation between aortic strain and left ventricular tissue Doppler echocardiographic parameters.

Variables	Co-efficient (p value)		
	Total IBD patients (n = 72)	UC patients (n = 56)	CD patients (n = 16)
Systolic myocardial wave (S′)	0.366 (0.001)	0.362 (< 0.001)	0.206 (0.098)
Early diastolic myocardial wave (E′)	0.531 (< 0.001)	0.522 (< 0.001)	0.374 (0.002)
Late diastolic myocardial wave (A′)	0.275 (0.002)	0.278 (0.004)	0.217 (0.080)
E/E′	–0.383 (< 0.001)	–0.379 (< 0.001)	–0.336 (0.006)
E′/A′	0.309 (0.001)	0.330 (0.001)	0.145 (0.246)
Myocardial isovolumetric contraction time	–0.364 (< 0.001)	–0.359 (< 0.001)	–0.331 (0.007)
Ejection time	0.386 (< 0.001)	0.391 (< 0.001)	0.355 (0.003)
Myocardial isovolumetric relaxation time	–0.507 (< 0.001)	–0.491 (< 0.001)	–0.470 (< 0.001)
Myocardial performance index	–0.567 (< 0.001)	–0.556 (< 0.001)	–0.574 (< 0.001)

IBD — inflammatory bowel disease; UC — ulcerative colitis; CD — Crohn's disease

Discussion

This is the first study designed to determine the relationship of AS with the LV function in IBD patients without known CV risk factors. There are three major results of this study: 1) stiffness of the aorta is increased in IBD patients, independent of atherogenic risk factors, including HT and aortic atherosclerosis; 2) IBD patients show sub-clinical LV diastolic and systolic dysfunction; 3) most importantly, there is a significant association between AS and both the LV systolic and diastolic function in these patients compared with matched healthy controls.

The aortic stiffness observed in IBD patients can be explained by several mechanisms. Recent studies have reported an association between chronic low-grade inflammation and arterial stiffening [12, 13]. Systemic inflammation thus appears to be an emerging causal factor for increased arterial stiffness in chronic inflammatory disease states, such as systemic lupus erythematosus [12] and rheumatoid arthritis [12]. Moreover, it has been reported that even acute, mild, transient inflammatory stimuli may cause deterioration of the elastic properties of large arteries [14]. However, the arterial stiffening noted in cases of chronic inflammatory disorders may be independent of the presence of atherosclerosis and related to disease duration [12] and/or, alternatively, present as a manifestation of preceding vascular disease. Several mechanisms by which a systemic inflammatory state can accelerate the atherosclerotic process have been suggested. Cytokine-mediated damage of the endothelium, immune cell activation

and stimulation of the coagulation cascade have all been implicated. The onset of IBD seems to be the result of a combination of environmental, genetic and immunologic factors in which an uncontrolled immune response within the intestine leads to the development of inflammation in genetically predisposed individuals [15]. Dysfunction of the intestinal immune system and cross-reactivity against host epithelial cells have further been implicated as major mechanisms by which inflammation occurs [16]. In a study of 70 patients with CD, it was shown that more than 20% of the subjects exhibited either chronic inflammatory-cell infiltration, acute and chronic inflammatory-cell infiltration, obliterative changes with inflammatory-cell infiltration or granulomatous inflammation in walls of the arteries or arterioles [17]. In the last decade, it has become increasingly evident that chronic systemic inflammation plays a pivotal role in the pathogenesis of atherosclerosis [18]. Early atherosclerosis is a clinical feature common to several inflammatory and immunological diseases [16]. Furthermore, findings of an increased carotid intima–media thickness (a measurement of the atherosclerotic burden), endothelial dysfunction and atherogenic alterations in the lipid profiles of patients with IBD have fueled the hypothesis suggesting a potential increased risk of atherosclerosis-driven vascular diseases in cases of IBD [19–21].

Likewise, an increased risk of CV diseases in patients with other inflammatory conditions, such as rheumatoid arthritis [22], psoriasis [23] and systemic lupus erythematous [24], independent of traditional CV risk factors, has been established. Currently, the reported results for the risk of CV disease in the setting of IBD have been ambiguous, with some studies revealing an increased risk of both ischemic heart disease and cerebrovascular accidents and others showing no associations [25–28]. Additionally, a few studies have suggested that IBD patients have a lower burden for some traditional risk factors for CV disease, such as HT, DM, dyslipidemia and obesity, and that non-traditional risk factors may play an important role in IBD patients [28, 29].

Coronary artery disease, DM, HT and thyroid dysfunction are clinical conditions causing increased AS [30]. Therefore, we excluded patients having these diseases from our study. Increased arterial stiffness gives rise to systolic HT, LV hypertrophy and impaired coronary perfusion, resulting in high CV risks. Moreover, increased AS is known to be an independent risk factor for CV morbidity and mortality [30].

Arterial stiffness can be evaluated using various methods, including applanation tonometry, PW velocity and transthoracic echocardiography (TTE). The PW velocity measured at the carotid and femoral arteries is considered to be the gold standard measurement of arterial stiffness [6]. However, M-mode echocardiography, as used in this study to evaluate AS, is a validated and reproducible method for conducting non-invasive assessments of arterial stiffness. Pulsatile alterations in the diameter of the aorta, as well as the degree of strain and distensibility, can be evaluated with the aid of TTE [31]. The easy availability and low costs of this modality are only some advantages of this method.

In the present study, the LV systolic and diastolic functions were evaluated using conventional echocardiographic techniques, including TDE. We used the E/A, E'/A' and E/E' ratios, the most important parameters, to evaluate the LV diastolic function. Moreover, we used MPI and Sm to assess the LV systolic function. These TDE parameters are less affected by the limiting variables of conventional echocardiographic methods, such as preload, afterload, ventricular geometry, BP and heart rate [32, 33]. We herein demonstrated that there was an increased rate of both systolic and diastolic dysfunction in IBD patients compared to the controls. Moreover, the aortic stiffness indices, ASt and distensibility were shown to be significantly lower in the patients than in the controls.

The findings of this study also showed a close association between AS and LV systolic and diastolic dysfunction. LV contractions lead to opening of aortic leaflets, which displaces the aortic annulus and generates a force that stretches the ascending aorta. The AS observed in IBD patients increases the usually ignored component of LV preload and results in myocardial stiffness, which causes gradual impairment of the LV function. LV dysfunction begins with diastolic dysfunction and progresses to systolic dysfunction. In our study, there was a significant relationship between ASt and AD and the E'/A' ratio, E/E' ratio, Sm and MPI in the patient group.

In the present study, we excluded subjects with HT, DM, dyslipidemia, cardiac and pulmonary problems and obesity in order to avoid the negative effects of these variables on the myocardium and aorta. A low BMI and lipid levels have been previously seen in IBD patients [34–37]. In our study, although statistically non-significant, the patients had lower BMI values than the controls in addition to significantly lower LDL-C levels.

Additionally, the number of smoking subjects was similar between the groups. We also analyzed relatively younger subjects under 50 years of age, and the subgroup analysis revealed nearly the same findings. Therefore, the abnormal findings of LV systolic and diastolic dysfunction and the increased AS noted in this study are assumed to be due to disease-related factors.

Limitations of the study

Some limitations of this study must be mentioned. The first and main limitation of this study is that we did not obtain any invasive measurements to evaluate the PP or elasticity of the aorta. However, although invasive methods remain the gold standard, several reports have demonstrated M-mode echocardiography to be a reliable alternative to such techniques. Indeed, the non-invasively calculated measurement of aortic elasticity exhibits excellent correlations with indices derived from invasive methods [38, 39]. Second, the relatively low number of subjects included in this study may prevent generalization of the results to all IBD patient populations. Therefore, large-scale studies are needed to confirm our results. Third, although a relatively small number of patients (16%) receiving immunosuppressive drugs and steroids were included in this study, these drugs might have negatively affected our results.

Conclusions

In the present study, it was shown that indices of AS are independently associated with echocardiographic parameters of the LV systolic and diastolic functions in patients with IBD without known CV risk factors. Aortic elasticity parameters measured using non-invasive echocardiography can be beneficial for predicting early CV risks in IBD patients. However, future large, prospective longitudinal studies are needed to determine the true risk of CV disease in IBD populations and further characterize preventive and risk factors.

Conflict of interest: None declared

References

1. Geerling BJ, Badart-Smook A, Stockbrügger RW, Brummer RJ. Comprehensive nutritional status in recently diagnosed patients with inflammatory bowel disease compared with population controls. Eur J Clin Nutr, 2000; 54: 514e21.
2. Levy E, Rizwan Y, Thibault L et al. Altered lipid profile, lipoprotein composition, and oxidant and antioxidant status in pediatric Crohn disease. Am J Clin Nutr, 2000; 71: 807e15.
3. Jahnsen J, Falch JA, Mowinckel P, Aadland E. Body composition in patients with inflammatory bowel disease: A population-based study. Am J Gastroenterol, 2003; 98: 1556e62.
4. Yarur AJ, Deshpande AR, Pechman DM, Tamariz L, Abreu MT, Sussman DA. Inflammatory bowel disease is associated with an increased incidence of cardiovascular events. Am J Gastroenterol, 2011; 106: 741e7.
5. Haapamäki J, Roine RP, Turunen U, Färkkilä MA, Arkkila PE. Increased risk for coronary heart disease, asthma, and connective tissue diseases in inflammatory bowel disease. J Crohns Colitis, 2011; 5: 41e7.
6. Laurent S, Cockcroft J, Van Bortel L et al. Expert consensus document on arterial stiffness: Methodological issues and clinical applications. Eur Heart J, 2006; 27: 2588–2605.
7. Zanoli L, Cannavò M, Rastelli S et al. Arterial stiffness is increased in patients with inflammatory bowel disease. J Hypertens, 2012; 30: 1775e81.
8. Ikonomidis I, Lekakis J, Stamatelopoulos K. Aortic elastic properties and left ventricular diastolic function in patients with Adamantiades-Behcet's disease. J Am Coll Cardiol, 2004; 43: 1075–1081.
9. Arnett DK, Evans GW, Riley WA. Arterial stiffness a new cardiovascular risk factor. Am J Epidemiol, 1994; 140: 669–682.
10. Eren M, Gorgulu S, Uslu N, Celik S, Dağdeviren B, Tezel T. Relation between aortic stiffness and left ventricular diastolic function in patients with hypertension, diabetes, or both. Heart, 2004; 90: 37–43.
11. Schiller NB, Shah PM, Crawford M. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardio-grams. J Am Soc Echocardiogr, 1989; 2: 358–367.
12. Roman MJ, Devereux RB, Schwartz JE et al. Arterial stiffness in chronic inflammatory diseases. Hypertension, 2005; 46: 194–199.
13. Booth AD, Wallace S, McEniery CM et al. Inflammation and arterial stiffness in systemic vasculitis: A model of vascular inflammation. Arthritis Rheum, 2004; 50: 581–588.
14. Vlachopoulos C, Dima I, Aznaouridis K et al. Acute systemic inflammation increases arterial stiffness and decreases wave reflection in healthy individuals. Circulation, 2005; 112: 2193–2200.
15. Karlinger K, Gyorke T, Mako E, Mester A, Tarjan Z. The epidemiology and the pathogenesis of inflammatory bowel disease. Eur J Radiol, 2000; 35: 154–167.
16. Yu Y, Sitaraman S, Gewirtz AT. Intestinal epithelial cell regulation of mucosal inflammation. Immunol Res, 2004; 29: 55–68.
17. Geller SA, Cohen A. Arterial inflammatory-cell infiltration in Crohn's disease. Arch Pathol Lab Med, 1983; 107: 473–475.
18. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med, 2005; 352: 1685–1695.
19. Theocharidou E, Gossios TD, Griva T et al. Is there an association between ınflammatory bowel diseases and carotid intima-media thickness? Preliminary data. Angiology 2014; 65: 543–550. doi: 10.1177/0003319713489876.
20. Roifman I, Sun YC, Fedwick JP et al. Evidence of endothelial dysfunction in patients with inflammatory bowel disease. Clin Gastroenterol Hepatol, 2009; 7: 175–182.
21. Van Leuven SI, Hezemans R, Levels JH et al. Enhanced atherogenesis and altered high density lipoprotein in patients with Crohn's disease. J Lipid Res, 2007; 48: 2640–2646.
22. Avina-Zubieta JA, Thomas J, Sadatsafavi M, Lehman AJ, Lacaille D. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis, 2012; 71: 1524–1529.

23. Patel RV, Shelling ML, Prodanovich S, Federman DG, Kirsner RS. Psoriasis and vascular disease-risk factors and outcomes: A systematic review of the literature. J Gen Intern Med, 2011; 26: 1036–1049.
24. Cervera R, Khamashta MA, Font J et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: A comparison of early and late manifestations in a cohort of 1,000 patients. Medicine (Baltimore), 2003; 82: 299–308.
25. Ha C, Magowan S, Accortt NA, Chen J, Stone CD. Risk of arterial thrombotic events in inflammatory bowel disease. Am J Gastroenterol, 2009; 104: 1445–1451.
26. Kristensen SL, Ahlehoff O, Lindhardsen J et al. Disease activity in inflammatory bowel disease is associated with increased risk of myocardial infarction, stroke and car-diovascular death: A Danish nationwide cohort study. PLoS One, 2013; 8: e56944.
27. Rungoe C, Basit S, Ranthe MF, Wohlfahrt J, Langholz E, Jess T. Risk of ischaemic heart disease in patients with inflammatory bowel disease: A nationwide Danish cohort study. Gut, 2013; 62: 689–694.
28. Yarur AJ, Deshpande AR, Pechman DM, Tamariz L, Abreu MT, Sussman DA. Inflammatory bowel disease is associated with an increased incidence of cardiovascular events. Am J Gastroenterol, 2011; 106: 741–747.
29. Sappati Biyyani RS, Fahmy NM, Baum E, Nelson KM, King JF. Inflammatory bowel disease and coronary artery disease. Indian J Gastroenterol, 2009; 28: 28–30.
30. Laurent S, Boutouyrie P, Asmar R et al. Aortic stiffness is an independent predictor of all cause and cardiovascular mortality in hypertensive patients. Hypertension, 2001; 37: 1236–1241.
31. Lacombe F, Dart A, Dewar E, Jennings G, Cameron J, Laufer E. Arterial elastic properties in man: A comparison of echo--Doppler indices of aortic stiffness. Eur Heart J, 1992; 13: 1040–1045.
32. De Boeck BW, Cramer MJ, Oh JK, Aa RP, Jaarsma W. Spectral pulsed tissue Doppler imaging in diastole: A tool to increase our insight in and assessment of diastolic relaxation of the left ventricle. Am Heart J, 2003; 146: 411–419.
33. Yu CM, Sanderson JE. Right and left ventricular diastolic function in patients with and without heart failure: Effect of age, sex, heart rate, and respiration on Doppler-derived measurements. Am Heart J, 1997; 134: 426–434.
34. Geerling BJ, Badart-Smook A, Stockbrugger RW, Brummer RJ. Comprehensive nutritional status in recently diagnosed patients with inflammatory bowel disease compared with population controls. Eur J Clin Nutr, 2000; 54: 514–521.
35. Levy E, Rizwan Y, Thibault L et al. Altered lipid profile, lipoprotein composition, and oxidant and antioxidant status in pediatric Crohn disease. Am J Clin Nutr, 2000; 71: 807–815.
36. Jahnsen J, Falch JA, Mowinckel P, Aadland E. Body composition in patients with inflammatory bowel disease: A population-based study. Am J Gastroenterol, 2003; 98: 1556–1562.
37. Yarur AJ, Deshpande AR, Pechman DM, Tamariz L, Abreu MT, Sussman DA. Inflammatory bowel disease is associated with an increased incidence of cardiovascular events. Am J Gastroenterol, 2011; 106: 741–747.
38. Stefanadis C, Dernellis J, Tsiamis E et al. Aortic stiffness as a risk factor for recurrent acute coronary events in patients with ischaemic heart disease. Eur Heart J, 2000; 21: 390–396.
39. Stefanadis C, Stratos C, Boudoulas H, Kourouklis C, Toutouzas P. Distensibility of the ascending aorta: Comparison of invasive and non-invasive techniques in healthy men and in men with coronary artery disease. Eur Heart J, 1990; 11: 990–996.