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Increased aortic stiffness in ulcerative colitis

Research Article

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Abstract: Introduction. Ulcerative colitis (UC) is a chronic inflammatory disease of the colon. Currently, there is an increased scientific interest in the evaluation of early functional vascular alterations, especially in inflammatory disorders. The present study was aimed to examine whether UC is associated with abnormalities in aortic elasticity. Methods. The study was comprised of 11 UC patients (mean age 39 ± 12 years, 7 males), their results were compared to 22 age- and gender-matched controls. All subjects underwent a complete two-dimensional transthoracic Doppler echocardiography including evaluation of aortic elastic properties. The oscillometry-based Arteriograph device was used in all cases to measure aortic pulse-wave velocity (PWV) and augmentation index (Aix). Results. Despite similar blood pressure values, aortic stiffness index, PWV and Aix were significantly increased, while pulsatile change in aortic diameter, aortic strain and aortic distensibility were significantly decreased in UC patients compared to controls. Conclusion. Abnormal echocardiographic aortic elastic properties and Arteriograph-derived pulse-wave velocity could be demonstrated in patients with ulcerative colitis.

Keywords: *Aortic • Stiffness • Distensibility • Ulcerative colitis*

1. Introduction

Ulcerative colitis (UC) is a chronic inflammatory disease of the colon [1]. The most common extra intestinal manifestations of UC are iritis, uveitis, primary sclerosing cholangitis, nodal erythema and pyoderma gangrenosum [2]. To date, complications within the cardiovascular system seem to be uncommon. There is increasing scientific interest in the evaluation of early functional vascular alterations, especially in inflammatory disorders [3]. There are a number of non-invasive method with which aortic distensibility could be determined including assessment of echocardiographic aortic elastic properties and pulse-wave velocity (PWV) / augmentation index (Aix) measurement by Arteriograph [4]. The present study was aimed at determining whether UC is associated with abnormalities in aortic elasticity.

2. Materials and methods

Study population. The study was comprised of 11 UC patients (mean age 39 ± 12 years, 7 males), their results were compared to 22 age- and gender-matched controls. Diagnosis of UC followed the available guidelines [5]. The study complied with the Declaration of Helsinki. Informed consent was obtained from each patient and the study was approved by the institutional review board at University of Szeged, Hungary. Systolic and diastolic blood pressures (SBP and DBP, respectively) were measured in the supine position with a mercury

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cuff sphygmomanometer from the left arm after 10 min of rest in accordance to the European Guidelines for the Management of Hypertension [6]. Blood pressure values were averaged from three consecutive measurements. None of the patients or control subjects used coffee or tea within one hour before blood pressure measurements and none of the patients or control subjects smoked.

Biochemical measurements. Blood samples were drawn by venipuncture to evaluate routine blood parameters following 8h fasting.

Transthoracic echocardiography. All subjects underwent a complete two-dimensional transthoracic Doppler echocardiography study using Toshiba Powervision 8000 and Aplio echocardiography equipments (Toshiba, Tokyo, Japan) in the left lateral decubitus position from multiple windows. All echocardiographic studies were digitally stored and evaluated by a single expert (HG) who was blinded to the clinical data. All echocardiographic measurements were averaged from 3 beats. M-mode echocardiography was used to measure LV internal dimensions. Aortic elastic properties were calculated according to the literature [4,7]. Systolic and diastolic ascending aortic diameters (SD and DD, respectively) were recorded in M-mode at a level of 3 cm above the aortic valve from a parasternal long-axis view (Figure 1A). The SD and DD were measured at the time out of maximum aortic anterior motion and at the peak of QRS complex, respectively. The aortic elasticity parameters was calculated as follows:

- Aortic strain = (SD – DD) / DD
- Aortic stiffness index (β) = ln (SBP / DBP) / [(SD - DD) / DD], where 'ln' is the natural logarithm.
- Aortic distensibility = 2 x (SD – DD) / [(SBP – DBP) x DD].

Pulse-wave assessment. The oscillometry-based Arteriograph device was used in all cases to measure aortic PWV and Aix [4,8-10]. It is based on the complete occlusion of the brachial artery by a simple cuff allowing recording and separation of pronounced early forward and late reflected systolic waves [8-10]. The time elapsed between the early and late systolic wave peaks (P1 and P2) equals the travel time of the forward aortic pulse wave to the bifurcation and its backward reflection to the observational site. The aortic length was estimated as the sternal notch / pubic bone distance and was used to determine aortic PWV. AIx is another measure of aortic stiffness and was calculated on the basis of the formula AIx% = [(P2-P1)/PP] x 100, where PP is the pulse pressure (Figure 1B).

Statistical analysis. Continuous variables were given as means ± standard deviation, while categorical variables were defined as percentage. Independent samples Student's t-test were used to compare continuous variables and chi square test to compare categorical ones. Numerical correlations were established by a Pearson's correlation. A value of $p < 0.05$ was considered statistically significant. Medcalc software (Medcalc, Mariakerke, Belgium) was used during statistical evaluations. Interobserver reproducibility for measuring aortic SD and DD using Bland-Altman method in our institution is 84 and 88%, respectively [11].

3. Results

Clinical data of UC patients and controls are presented in Table 1. Despite similar blood pressure values, aortic stiffness index, PWV and Aix were significantly increased, while pulsatile change in aortic diameter, aortic strain and aortic distensibility were significantly

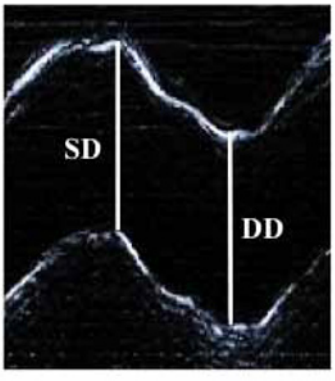

Figure 1. Measurement of systolic (DS) and diastolic (DD) ascending aortic diameter is presented on an M-mode echocardiographic image obtained at a level 3 cm above the aortic valve (Figure 1A).

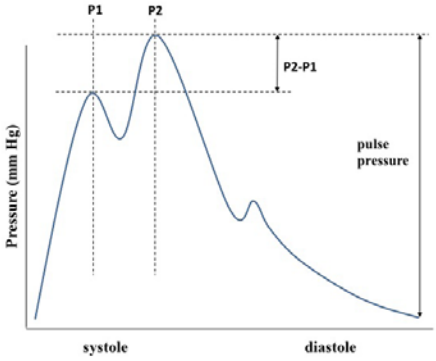

Figure 2. An Arteriography-derived oscillometric pulse wave is presented, where P1 is the pressure peak of the initial wave in mm Hg and P2 is the pressure pressure peak of the reflected wave in mm Hg.

Table 1. Clinical data of patients with ulcerative colitis and that of controls

	UC patients	Controls
N	11	22
Age (years)	39.0 ± 11.5	38.8 ± 10.9
Males (%)	7 (64)	11 (50)
Diabetes mellitus (%)	0 (0)	0 (0)
Hypertension (%)	1 (9)	2 (9)
Smoking (%)	2 (18)	5 (23)
Body mass index (kg/m^2)	27.4 ± 4.1	26.4 ± 5.2
Triglycerides (mg/dl)	138 ± 58	132 ± 52
C reactive protein (mg/dl)	0.81 ± 1.30*	0.25 ± 0.21
Immunosuppressive medication (%)	1 (9)	0 (0)

*Continuous variables are given as mean ± standard deviation. Abbreviations. UC : ulcerative colitis * p <0.05 vs. controls*

Table 2. Blood pressure and echocardiographic data of patients with ulcerative colitis and that of controls

	UC patients	Controls
Blood pressure values		
Systolic blood pressure (mm Hg)	124.2 ± 18.2	123.0 ± 8.68
Diastolic blood pressure (mm Hg)	78.9 ± 9.9	73.8 ± 7.2
Aortic pulse pressure (mm Hg)	45.3 ± 9.9	49.2 ± 8.2
Echocardiographic data		
LV end-diastolic diameter (mm)	50.3 ± 4.4	48.4 ± 4.6
LV end-systolic diameter (mm)	32.6 ± 3.5	29.9 ± 4.0
LV mass index (g/m^2)	98 ± 21	100 ± 25
LV ejection fraction (%)	62.3 ± 4.7	68.3 ± 5.8
Interventricular septum (mm)	9.4 ± 1.8	9.0 ± 1.0
LV posterior wall (mm)	9.2 ± 1.1	8.9 ± 0.8
Aortic systolic diameter (DS) (mm)	29.8 ± 4.4	28.9 ± 2.0
Aortic diastolic diameter (DD) (mm)	28.5 ± 5.0	26.3 ± 2.4
Pulsatile change in aortic diameter (mm)	1.35 ± 1.13*	2.61 ± 1.36
Aortic strain	0.054 ± 0.055*	0.102 ± 0.058
Aortic distensibility (cm^2/dynes 10^{-6})	1.78 ± 1.71*	3.17 ± 1.75
Aortic stiffness index	16.2 ± 10.2*	6.46 ± 3.43
Arteriography results		
PWV (m/s)	9.17 ± 1.59*	7.65 ± 1.42
AIx	-15.7 ± 18.6*	-43.4 ± 26.6

*Continuous variables are given as mean ± standard deviation. Abbreviations. LV : left ventricular, UC : ulcerative colitis * p <0.05 vs. controls*

decreased in UC patients compared to controls (Table 2). There was not any significant correlation between C reactive protein level and vascular elasticity parameters.

4. Discussion

Increased vascular stiffness is an index of vascular health, an early sign of vascular dysfunction and a predictor of adverse cardiovascular outcomes. Arterial stiffening and its hemodynamic consequences can be easily and reliably measured using a wide range of non-invasive techniques. In prior studies it has been shown that pulsatile changes in ascending aortic diameter can be measured during routine transthoracic echocardiography and by using forearm blood pressure values several echocardiographic aortic elastic properties could be assessed [4,7]. Stefanadis et al. described that such noninvasive measurements of aortic elastic properties by echocardiography are as accurate as invasive methods [7]. PWV and Aix are another two major characteristics of arterial stiffness, their measurement by Arteriograph has recently been validated [4,8-10].

In recent studies the importance of inflammation on the pathogenesis of arterial stiffness has been highlighted [3,12]. From inflammatory disorders, it is mainly chronic rheumatic disorders that have been examined to be associated with increased arterial stiffness [13,14]. In the present study, the echocardiographically determined aortic elastic properties and Arteriograph-derived PWV and Aix were found to be abnormal in UC patients compared to age- and gender-matched healthy controls. These findings confirm previous reports demonstrating increased Sphygmocor-derived carotid-femoral PWV

based on applanation tonometry in UC patients [15]. Increased carotid intima-media thickness has also been found in this study.

Several vascular complications have been described associated with UC including different forms of aortitis [16], vasculitis [17], capillaritis [18] and panniculitis with vasculitis [19]. There are several reports showing a combination of Takayasu's arteritis and UC [20,21]. Activation of coagulation system could develop in some patients with aortic [22-25], retinal artery [26], splanchnic artery, portal vein [27] and pulmonary artery [28] embolism, and disseminated intravascular coagulopathy (DIC) [29]. Moreover association between UC and aortic aneurysm could be demonstrated in some patients [30].

Limitations. The effects of medications, inflammation parameters and other UC specific alterations on aortic elastic properties were not examined in this study. Only a limited number of patients and controls were evaluated.

Conclusions. Despite a low number of UC patients examined, it could be concluded that alterations in aortic elasticity could be demonstrated in patients with ulcerative colitis.

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