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Aortic stiffness in patients with inflammatory bowel diseases

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AIM: Inflammation is an independent risk factor for cardiovascular disease (CVD). CVD risk in patients with inflammatory bowel diseases (IBD) has been investigated in few studies with contradictory results. Aortic stiffness, assessed by measuring pulse wave velocity (PWV), is associated with CVD risk. The aim of this study was to assess carotid-femoral PWV in patients with IBD without history of CVD compared with controls.

MATERIAL-METHODS: Traditional CVD risk factors and IBD characteristics were assessed in 66 patients with IBD, 43 with Crohn's disease (CD) and 23 with ulcerative colitis (UC), and 44 controls. PWV was measured using the SphygmoCor system. Parameters associated with PWV were identified by linear regression.

RESULTS: There were 29 men (43.9%) in the IBD group and 20 (45.5%) in the control group. The median age was 38 years in both groups. There were 32 smokers (48.5%) in the IBD group and 20 (45.5%) in the control group. 60% of patients had mild disease pattern, and 74% were in remission at the time of the study. IBD patients had lower haemoglobin, total cholesterol, low density lipoprotein cholesterol (LDL-C) and folic acid levels, and higher platelet count. There was no difference in PWV between patients and controls (6.6 ±1.3 vs 6.1±0.9 m/s; p=0.247), or between patients

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ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

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Η αορτική σκληρία σε ασθενείς με φλεγμονώδη νοσήματα του εντέρου

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ΣΚΟΠΟΣ: Η φλεγμονή αποτελεί ανεξάρτητο παράγοντα καρδιαγγειακού (ΚΑ) κινδύνου. Ο ΚΑ κίνδυνος έχει μελετηθεί σε ασθενείς με φλεγμονώδεις παθήσεις του εντέρου (ΦΝΕ) με αντικρουόμενα αποτελέσματα. Η αορτική σκληρία, η οποία εκτιμάται με τη μέτρηση της ταχύτητας διάδοσης του σφυγμικού κύματος (pulse wave velocity, PWV), συσχετίζεται με τον ΚΑ κίνδυνο. Σκοπός της μελέτης είναι η μέτρηση της PWV μεταξύ καρωτίδας και μηριαίας αρτηρίας σε ασθενείς με ΦΝΕ χωρίς ιστορικό ΚΑ νόσου σε σύγκριση με μια ομάδα μαρτύρων.

ΥΛΙΚΟ-ΜΕΘΟΔΟΣ: Έγινε εκτίμηση των κλασικών παραγόντων ΚΑ κινδύνου και των χαρακτηριστικών των ΦΝΕ σε 66 ασθενείς με ΦΝΕ, 43 με νόσο του Crohn (ΝC) και 23 με ελκώδη κολίτιδα (ΕΚ), και σε 44 μάρτυρες. Η μέτρηση της PWV έγινε με το σύστημα SphygmoCor. Διερευνήθηκαν οι παράμετροι που συσχετίζονται με την PWV με την εφαρμογή linear regression.

ΑΠΟΤΕΛΕΣΜΑΤΑ: Συμπεριελήφθησαν στη μελέτη 29 άνδρες (43.9%) στην ομάδα των ΦΝΕ και 20 (45.5%) στην ομάδα των μαρτύρων. Η μέση ηλικία ήταν 38 έτη κα στις δύο ομάδες. Υπήρχαν 32 καπνιστές (48.5%) στην ομάδα των ΦΝΕ και 20 (45.5%) στην ομάδα των μαρτύρων. Το 60% των ασθενών είχε ήπια δραστηριότητα νόσου και το 74% ήταν σε ύφεση κατά την περίοδο της μελέτης. Οι ασθενείς με ΦΝΕ είχαν χαμηλότερη τιμή αιμοσφαιρίνης, ολικής χοληστερόλης, χοληστερόλη χα-

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with CD and UC (6.8±1.3 vs 6.3±1.1 m/s; p=0.108), although smoking rates were significantly higher in CD patients. Factors associated with PWV were age, BMI, mean arterial pressure and smoking, with age making the greater unique contribution.

CONCLUSIONS: Our study showed no difference in PWV between patients with IBD and controls. This might be due to lack of association between IBD and CVD risk, or the inclusion of patients with low inflammatory burden and low LDL-C, which are less likely to exhibit early arterial wall changes. Further studies are required to investigate such an association.

μηλής πυκνότητας λιποπρωτεϊνών (LDL-C) και φυλικού οξέος, και υψηλότερες τιμές αιμοπεταλίων. Δεν βρέθηκε διαφορά ως προς την PWV μεταξύ των ασθενών και των μαρτύρων (6,6±1,3 vs 6,1±0,9 m/s, p=0,247), ή μεταξύ των ασθενών με ΝC και ΕΚ (6,8±1,3 vs 6,3±1,1 m/s, p=0,108), αν και η συχνότητα του καπνίσματος ήταν σημαντικά υψηλότερη στους ασθενείς με ΝC. Οι παράγοντες που συσχετίσθηκαν με την PWV ήταν η ηλικία, ο δείκτης μάζας σώματος, η μέση αρτηριακή πίεση και το κάπνισμα, από τους οποίους η ηλικία είχε την ισχυρότερη συσχέτιση.

ΣΥΜΠΕΡΑΣΜΑΤΑ: Δεν βρέθηκε διαφορά στην ταχύτητα διάδοσης του σφυγμικού κύματος μεταξύ ασθενών με ΦΝΕ και των μαρτύρων. Αυτό μπορεί να οφείλεται είτε στην απουσία συσχέτισης μεταξύ ΦΝΕ και ΚΑ κινδύνου, είτε στη συμμετοχή στη μελέτη ασθενών με χαμηλό φορτίο φλεγμονής και χαμηλή LDL-C, οι οποίοι είναι λιγότερο πιθανό να έχουν πρώιμες αλλαγές στο αρτηριακό τοίχωμα. Θα χρειασθούν περισσότερες μελέτες για να διερευνηθεί περαιτέρω μια τέτοια συσχέτιση.

Λέξεις ευρετηρίου: Inflammatory bowel diseases, cardiovascular disease, aortic stiffness, pulse wave velocity, atherosclerosis.

Key words: Φλεγμονώδεις παθήσεις του εντέρου, καρδιαγγειακή νόσος, αορτική σκληρία, ταχύτητα διάδοσης σφυγμικού κύματος, αθηροσκλήρωση.

1. Introduction

Atherosclerosis, with main clinical manifestations coronary artery disease (CAD), cerebrovascular disease and peripheral artery disease, is a leading cause of morbidity and mortality in Western world.[1,2] High cholesterol levels, in particular low-density lipoprotein cholesterol (LDL-C), represent a principal risk factor for cardiovascular disease (CVD). Atherogenesis was initially considered plain accumulation of lipids within the arterial wall, before being recognized as an inflammatory process.[3] Furthermore, activation of the arterial wall inflammation contributes to plaque rupture and elicits acute coronary syndromes.[4]

Inflammation is an independent risk factor for atherosclerosis.[5] The association between CVD and two chronic inflammatory diseases, rheumatoid arthritis(RA) and systemic lupus erythematosus (SLE), is well established.[6] Several mediators have been implicated, including interleukin 6, phospholipase A_2 and tumor necrosis factor a, that enhance endothelial dysfunction, impair endothelial restoration and favor the formation and rupture of the atheromatous plaque.[7]

Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are associated with increased risk of thromboembolism, in particular venous thrombotic events and pulmonary embolism.[8] These complications are likely attributable to a hypercoagulable state and high homocysteine levels, which are common in IBD.[9] The association between IBD and CVD has been assessed in few retrospective studies. The prevalence of CAD was greater compared to general population in all but one study.[10–13] The risk of CAD in a Danish cohort of about 29,000 IBD patients was 1.6-fold increased, particularly in the first year after IBD diagnosis.[13] Although these results imply an association between IBD and the risk of CAD, there are several limitations, mainly related to the accuracy of retrospective assessment of CVD risk factors (the prevalence of smoking was not assessed in several of these studies) and events.

Aortic stiffness is a surrogate marker of atherosclerosis and an important predictor of CVD events.[14] Arterial stiffness is increased when the elastic properties of the arterial wall are reduced, resulting mainly from the replacement of elastin with collagen and vascular smooth muscle cell hypertrophy. These changes accelerate atherogenesis. Pulse wave velocity (PWV), i.e. the speed at which the pressure waveform travels along the aorta and large arteries during each cardiac cycle, is the gold standard for the assessment of arterial stiffness.

Carotid-femoral PWV is the most commonly used measurement. Augmentation index (AIx) represents the extra pressure caused by pressure wave reflection back from the periphery. It is influenced not only by arterial stiffness but mostly by the intensity of wave reflections. AIx is an indirect surrogate of arterial stiffness.[14]

The single published study that assessed PWV in 32 adult patients with IBD and 32 healthy controls, showed increased carotid-femoral PWV in the former (6.6±1.4 m/s *vs* 6±0.8, p<0.05).[15] Parameters that correlated with PWV were age and IBD duration.

The aim of our study was to: a) assess PWV in a group of patients with IBD compared with a control group, b) compare patients with CD and UC with regard to PWV, and c) assess factors associated with PWV.

2. Material-Methods

2.1. Patients and controls

The study group included 66 patients with IBD, 43 with CD and 23 with UC and 44 controls, 18 to 60 years old. These were consecutive patients that attended the IBD Outpatient Clinic at Hippokration General Hospital, Thessaloniki, Greece. The diagnosis of IBD was established based on clinical, laboratory, radiological, endoscopic and histological criteria. Exclusion criteria were history of coronary, peripheral artery or cerebrovascular disease, diabetes mellitus, chronic renal failure, familial dyslipidaemias, collagen tissue diseases and total proctocolectomy for UC.

On the day of the assessment, a detailed medical history and IBD history were obtained, physical examination was performed, blood pressure (BP) was measured; body weight and height were recorded. Blood samples were obtained after overnight fast to measure haemoglobin, white blood cells, platelets, C-reactive protein (CRP), total cholesterol, high-density lipoprotein cholesterol (HDL-C), LDL-C, triglycerides, vitamin B_{12}, folic acid, and homocysteine levels. PWV and AIx were measured as described below.

The study protocol was approved by the Aristotle University Ethics Committee, and all participants signed an informed consent form before inclusion in the study.

3. IBD activity

With regards to IBD history the following parameters were recorded: disease duration, extent of intestinal involvement (left-sided colitis, extensive colitis and pancolitis for UC; terminal ileitis, colitis, both terminal ileitis and colitis for CD), previous intestinal surgery, and number of flares in the previous 2 years. We arbitrarily classified disease activity as mild, moderate and severe, if there were up to 1, 2 to 3 and 4 or more flares, respectively, during the last 2 years. The Mayo score was calculated in patients with UC and the Crohn's Disease Activity Index (CDAI) in those with CD.[16,17] Remission was defined as CDAI≤150 for CD or Mayo score ≤2 for UC. Current medical treatment was also recorded.

4. CVD risk factors

The following established CVD risk factors were recorded: age, gender, cigarette smoking, hypertension, dyslipidaemia, obesity and family history of premature CVD. Smokers were further classified as light smokers (<20 pack years) or moderate-heavy smokers (>20 pack years) in keeping with the WHO classification (http://www.who.int/tobacco/en). Non-smokers were classified as never-smokers and former-smokers. Cut-off levels for BP and lipid levels were determined in accordance to respective guidelines,[18,19] corresponding to a low risk population such as the one in our study. The cut-off used for systolic BP was 140 mmHg and for diastolic BP 90 mmHg.[19] Mean arterial blood pressure (MAP) was calculated using the formula MAP=diastolic BP+(systolic BP-diastolic BP)/3. The cut-off used for total cholesterol was 200 mg/dL, for HDL-C 40 mg/dL and for LDL-C 130 mg/dL.[18] The use of antihypertensive and lipid-lowering agents was included in the definition of hypertension and dyslipidaemia, respectively. BMI was calculated as kg/m^2. Family history of premature CVD was defined as CVD in a male first-degree relative <55 years or in a female first-degree relative <65 years. Subjects with diabetes mellitus were excluded.

5. Aortic stiffness

Carotid-femoral PWV and AIx were assessed using the SphygmoCor system (ArtCor, Sydney, Australia). With the subject in the supine position, arterial pulse was recorded on the right carotid and subsequently on the right femoral artery using an applanation tonometer that was applied on the skin. The distance between the sites of recording was measured. PWV was calculated as the distance between carotid and femoral recording sites divided by the time delay between the feet of the carotid and femoral pressure waveforms (m/s). To assess AIx the radial artery waveform was recorded using the applanation tonometer. AIx was defined as the difference between the second and first systolic peaks expressed as the percentage of the pulse pressure.

6. Statistical analysis

Data were expressed as mean and standard deviation (SD) for continuous and normally distributed variables, median and range for continuous variables without

normal distribution, or frequencies (percentage) for categorical variables. We compared patients with controls, as well as CD patients with UC patients, with regard to established CVD risk factors, laboratory variables, PWV and AIx. For comparisons the chi-square test was used for categorical variables, the Student's t test and the Mann-Whitney test for continuous variables with or without normal distribution, respectively. Pearson (r) and Spearman (rho) correlation coefficient were calculated to identify significant correlations between PWV and different variables. Linear regression was applied to assess if the set of the variables that showed significant correlation with PWV could predict PWV, and to identify which one of them was the best predictor of PWV. The assumptions of multicollinearity, singularity, normality, linearity, homoscedasticity, and independence of residuals were checked before applying linear regression. The level of statistical significance was set at $p \leq 0.05$. Statistical analysis was performed using the Statistical Package for Social Sciences, version 20 (SPSS, IL, Chicago).

7. Results

7.1. Patients and controls

Sixty six patients with IBD, 43 with CD and 23 with UC, and 44 controls were included in the study. There were 29 men (43.9%) in the IBD group and 20 (45.5%) in the control group. The median age was 38 years in both groups. There were 32 smokers (48.5%) in the IBD group and 20 (45.5%) in the control group. The median BMI was 23.7 kg/m^2 and 24.3 kg/m^2, respectively. No patient or control had history of diabetes mellitus. There was no difference in MAP, history of hypertension, hyperlipidaemia or family history premature CVD between the 2 groups. Characteristics of patients and controls with regard to CVD risk are shown in table 1.

IBD patients had significantly lower haemoglobin levels (12.7±2.3 *vs* 13.8±1.3 g/L, p=0.003), higher platelet count (median 287 *vs* 210x109/L, p<0.0005), lower cholesterol levels (174.8±45.3 *vs* 204.2±38.1 mg/dL, p=0.001), lower LDL-C (106.3±35.4 *vs* 132.5±33.6 mg/dL, p<0.0005) and lower folic acid levels (median 5.3 vs 7.1 ng/mL, p=0.017). There was no difference in white cell count, CRP, HDL-C, triglycerides, vitamin B_{12} and homocysteine levels. Laboratory results for patients and controls are shown in table 2.

There was no significant difference in PWV (6.6±1.3 *vs* 6.1±0.9 m/s, p=0.247) and AIx (14.8±15.5 *vs* 15.6±16%, p=0.802) between patients with IBD and controls.

8. Patients with CD and UC

Mean disease duration was 8.4±6.7 years. Thirty nine patients (59.1%) had mild disease, 12 (18.2%) moderate, and 15 (22.7%) had severely active disease. Forty nine patients (74.2%) were in remission at the time of the study. There were no significant differences in disease duration and activity, and rate of remission between patients with CD and UC. Twelve patients with CD had previous intestinal surgery, but no patient with UC had surgery. Significantly more patients with UC were treated with 5-aminosalicylates. IBD characteristics are shown in table 3.

There were no significant differences in age, gender, BMI, MAP or family history of premature CVD between patients with CD and UC. The majority of CD patients (67.4%) were current smokers, whereas only 3 patients with UC (13%) were smokers (p<0.0005) (table 4).

With regards to laboratory parameters, patients with CD had lower vitamin B_{12} (median 271 *vs* 385 pg/mL, p=0.01) and folic acid levels (median 4.4 *vs* 7 ng/mL, p=0.011) compared with UC patients. There were no significant differences in the other laboratory parameters (table 5).

There was no significant difference in PWV (6.8±1.3 vs 6.3±1.1 m/s, p=0.108) and AIx (median 20 *vs* 10%, p=0.3) between patients with CD and UC. There was no difference among patients with mild, moderate or severe disease activity pattern, or between those in remission and those with active intestinal inflammation at the time of the study.

9. Predictors of PWV

Parameters that correlated with PWV were age (rho=0.494, p<0.0005), BMI (rho=0.356, p<0.0005), MAP (r=0.399, p<0.0005), and smoking (rho=0.247, p=0.01). In multivariate linear regression only age (beta 0.430, p=0.002) remained significant predictor of PWV. The above set of variables predicted 47.7% of the variance in PWV (p<0.0005).

10. Discussion

Our study showed that carotid-femoral PWV, an important surrogate of aortic stiffness, is not increased in patients with IBD compared with a control group with similar traditional CVD risk factors. There was no difference in PWV between patients with CD and UC. Parameters that associated with PWV were age, BMI, MAP and smoking, with age making the most significant contribution to PWV.

The single previous study that assessed PWV in IBD patients showed increased carotid-femoral PWV and

Table 1. Cardiovascular risk factors in patients with IBD and controls.

	IBD patients	Controls	p-value
Number	66	44	
Gender (%)			
• Male	29 (43.9)	20 (45.5)	NS
• Female	37 (56.1)	24 (54.5)	
Age (years)	38 (18–60)	38 (22–60)	NS
Smoking (%)	32 (48.5)	20 (45.5)	NS
Smokers (%)			
• Non-smokers	24 (36.4)	16 (36.4)	
• Former	9 (13.6)	8 (18.2)	NS
• Light	12 (18.2)	6 (13.6)	
• Heavy	21 (31.8)	14 (31.8)	
BMI (kg/m^2)	23.7 (16.5–37.2)	24.3 (18.3–34.2)	NS
Hypertension (%)	2 (3)	4 (9.1)	NS
MAP (mmHg)	86.3 (61.7–106.7)	86.2 (41.3–113.3)	NS
Hyperlipidaemia (%)	0	4 (9.1)	NS
Family history (%)	20 (30.3)	9 (20.5)	NS

BMI, body mass index; MAP, mean arterial pressure; NS, non significant

Table 2. Laboratory investigations in patients with IBD and controls.

	IBD patients	Controls	p-value
Haemoglobin (g/dL)	12.7±2.3	13.8±1.3	0.003
White blood cells (x10^9/L)	7 (3.1–13.6)	6.6 (3.5–12.5)	NS
Platelets (x10^9/L)	287 (118–580)	210 (135–346)	<0.0005
CRP (mg/L)	3.4 (0–160)	3.3 (3.2–13.4)	NS
Total cholesterol (mg/L)	174.8±45.3	204.2±38.1	0.001
HDL-C (mg/L)	48.1±14.1	52.1±14.6	NS
LDL-C (mg/L)	106.3±35.4	132.5±33.6	<0.0005
Triglycerides (mg/L)	101±47.2	98.4±50.3	NS
Vitamin B_{12} (pg/L)	323 (57–2000)	314 (131–985)	NS
Folic acid (ng/L)	5.3 (1.3–24)	7.1 (2.5–19.5)	0.017
Homocysteine (μmol/L)	13.1 (5.2–41)	13 (5.2–23.4)	NS

IBD, inflammatory bowel disease, CRP, C-reactive protein, HDL-C, high density lipoprotein cholesterol, LDL-C, low density lipoprotein cholesterol, NS, non significant

AIx in IBD patients compared with a group of healthy controls. This was a small study that included 32 patients with IBD (16 with CD and 16 with UC), 18-49 years old, without CVD risk factors.[15] The majority of patients (88%) were in remission at the time of the evaluation. However, no data were provided on disease activity overall, such as the number and severity of flares in the past, and the extent of intestinal involvement. This is particularly important as the inflammatory burden is the result of disease extent, duration, activity, and treatment that aims to suppress intestinal inflammation. In addition, although current smokers were excluded from the study, there were no data on the proportion of ex-smokers, which may have accounted for the difference in PWV, as smoking has a well-known impact on endothelial function and arterial wall properties.

In our study 74% of IBD patients were in remission, but most importantly 60% had mildly active disease overall, as assessed by the number of flares during the last two years. Furthermore, a significant proportion of patients were treated with infliximab, a highly potent anti-inflammatory agent, that may have accounted for lower inflammatory burden in our study group. Finally, LDL-C, a cardinal CVD risk factor, was significantly lower in patients with IBD. The very low LDL-C levels in IBD patients might be the result of intestinal malabsorption,

Table 3. Disease characteristics in patients with IBD.

	All IBD patients	Crohn's disease (n=43)	Ulcerative colitis (n=23)	p-value
Disease duration (years)	8.4±6.7	7 (1–26)	7 (1–28)	NS
Activity (%)				
• Mild (0–1 flares/2 years)	39 (59.1)	26 (60.5)	13 (56.5)	
• Moderate (2–3)	12 (18.2)	9 (20.9)	3 (13)	NS
• Severe (≥4)	15 (22.7)	8 (18.6)	7 (30.4)	NS
Remission (%)	49 (74.2)	33 (76.7)	16 (69.6)	NS
Disease extent-UC				
• Left-sided colitis	12			
• Extensive colitis	4			
• Pancolitis	7			
Disease extent-CD				
• Terminal ileum	20			
• Colon	9			
• Terminal ileum and colon	11			
CDAI	50.6±45.5			
Mayo score	2.85±3.4			
Previous surgery (%)	12 (19)	12 (30)	0	0.010
Treatment (%)				
• 5-ASA	39 (56.1)	17 (39.5)	20 (87)	0.001
• Azathioprine	35 (53)	21 (48.8)	14 (60.9)	NS
• Anti-TNF-a	29 (43.9)	21 (48.8)	8 (34.8)	NS
• Corticosteroids	12 (18.2)	6 (14)	6 (26.1)	NS

IBD, inflammatory bowel diseases, UC, ulcerative colitis, CD, Crohn's disease, CDAI, Crohn's disease activity index, 5-ASA, 5-aminosalicylates, TNF-a, tumor necrosis factor a, NS, non significant.

in particular in those with CD, dietary habits or the effect of chronic inflammation on lipid concentrations.[20] The above parameters, i.e. low inflammatory burden and lower LDL-C, should be taken into consideration in order to interpret the lack of difference in aortic stiffness between IBD patients and controls in our study.

Early changes in the arterial wall have also been assessed in patients with IBD by measuring carotid intima-media thickness (cIMT).[21–26] Plaque formation is the result of long-standing changes in the arterial wall, which can be detected before becoming clinically evident. cIMT is associated with CVD risk factors, as well with the risk of CVD events, thus it is widely used as a surrogate marker of atherosclerosis.[27] The studies of cIMT in IBD patients were, however, inconclusive, with half of them showing increased cIMT in IBD patients and the rest no difference compared with controls. The interpretation of these results is hampered by the small number of patients, the heterogeneity of the study populations with regards to inflammatory burden and smoking habits, and the lack of strict matching with controls.[28]

The incidence of CVD and/or CVD events has been assessed in retrospective cohorts, with the majority showing increased incidence in IBD patients.[10–13,29] As discussed above, in a Danish cohort of about 29,000 IBD patients there was 1.6-fold increased risk of CAD, in particular in the first year after IBD diagnosis was established.[13] This study had some important limitations, which also apply to the other cohort studies. The major limitation is related to the accuracy of CVD risk factor assessment, as there were no data on 2 major risk factors, i.e. smoking and BMI. Even though BMI is usually low in patients with IBD, this is not the case with smoking, which may represent an important component of CVD risk in IBD. Smoking seems to have a beneficial effect on intestinal inflammation in UC, and its cessation has been associated with exacerbations of intestinal inflammation and increased risk of colectomy.[30] In contrast, in CD smoking may be associated with disease flares.[31] A study in 820 patients with IBD showed increased prevalence of smoking among CD patients, whereas UC patients were more likely to be non-smokers or ex-smokers.[32] These differences in smoking rates may account for increased CVD risk in certain subgroups of IBD patients.[33] The second limitation is associated with the accuracy of the retrospective recording of CVD events, as methods used to extract data are not always accurate (for example, questionnaires mailed to patients). Another aspect of the problem is that increased rates of CVD may reflect

Table 4. Traditional cardiovascular risk factors in patients with Crohn's disease and ulcerative colitis.

	Crohn's disease (n=43)	Ulcerative colitis (n=23)	p-value
Gender (%)			
• Male	18 (41.9)	11 (47.8)	
• Female	25 (58.1)	12 (52.2)	NS
Age (years)	37.9±9.5	35±11.5	NS
Smoking (%)	29 (67.4)	3 (13)	<0.0005
Smokers (%)			
• Non-smokers	7 (16.3)	17 (73.9)	
• Former	6 (14)	3 (13)	<0.0005
• Light	11 (25.6)	1 (4.3)	
• Heavy	19 (44.2)	2 (8.7)	
BMI (kg/m^2)	23.7 (16.5–37.2)	23.9 (17.8–36.6)	NS
Hypertension (%)	2 (4.7)	0	NS
MAP (mmHg)	86.4±11.1	87.6±9.6	NS
Hyperlipidaemia (%)	0	0	
Family history (%)	13 (30.2)	7 (30.4)	NS

BMI, body mass index, MAP, mean arterial pressure, NS, non significant.

Table 5. Laboratory investigations in patients with Crohn's disease and ulcerative colitis.

	Crohn's disease	Ulcerative colitis	p value
Haemoglobin (g/dL)	13±2	12.3±2.7	NS
White blood cells (x10^9/L)	7.7±2.3	6.7±1.8	NS
Platelets (x10^9/L)	277±73	291±107	NS
CRP (mg/L)	5.2 (0–160)	3.2 (0.1–36.2)	NS
Total cholesterol (mg/L)	172 (63–259)	189 (91–268)	NS
HDL-C (mg/L)	46.2±15.4	51.2±11.6	NS
LDL-C (mg/L)	102.5±36.2	112.1±34.2	NS
Triglycerides (mg/L)	99.1±44.9	104.1±52.1	NS
Vitamin B_{12} (pg/L)	271 (57–762)	385 (195–2000)	0.010
Folic acid (ng/L)	4.4 (1.3–24)	7 (4.1–24)	0.011
Homocysteine (μmol/L)	13.3 (5.2–41)	11.9 (6–18.7)	NS

CRP, C-reactive protein, HDL-C, high density lipoprotein cholesterol, LDL-C, low density lipoprotein cholesterol, NS, non significant.

the closer medical surveillance that IBD patients receive, as suggested by the higher incidence of CAD in the first few months after IBD diagnosis in the Danish cohort. Therefore, although several studies demonstrate increased incidence of CVD in patients with IBD, their limitations do not allow definitive conclusions.

Chronic systemic inflammation is an independent CVD risk factor, as is clearly indicated by the paradigm of rheumatologic disorders such as SLE, RA and psoriasis. IBD are also characterized by chronic systemic inflammation with extra-intestinal manifestations. Thus, it could be supported that IBD are associated with increased CVD risk that parallels rheumatologic diseases. However, IBD patients exhibit some unique features such as smoking pattern, lower BMI, and dietary habits, which may alter this association. In order to elucidate a potential association between IBD and CVD risk, prospective studies with sufficient number of patients and long-term follow-up are needed. In addition, thorough assessment of traditional CVD risk factors, as well as patient stratification according to type of disease, inflammatory burden, and type of treatment, is required.

In conclusion, our study showed no difference in aortic stiffness between patients with IBD and controls. Mild disease activity, the use of highly potent anti-inflammatory agents and low LDL-C levels may have ameliorated the effect of chronic inflammation on arterial wall properties. Future studies should include patients with more severe disease activity and thus higher inflammatory burden.

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