



Original research article

## Cardiac and autonomic function in patients with Crohn's disease during remission



Monika Zawadka-Kunikowska<sup>a,\*</sup>, Joanna Słomko<sup>a</sup>, Maria Kłopotcka<sup>b</sup>, Ariel Liebert<sup>b</sup>,  
Małgorzata Tafil-Klawe<sup>c</sup>, Jacek J. Klawe<sup>a</sup>, Julia L. Newton<sup>d</sup>, Paweł Zalewski<sup>a</sup>

<sup>a</sup> Department of Hygiene, Epidemiology and Ergonomy, Nicolaus Copernicus University, Torun, Poland

<sup>b</sup> Department of Vascular Diseases and Internal Medicine, Nicolaus Copernicus University, Torun, Poland

<sup>c</sup> Department of Human Physiology, Nicolaus Copernicus University, Torun, Poland

<sup>d</sup> Institute of Cellular Medicine, The Medical School, Newcastle University, Newcastle-upon-Tyne, United Kingdom

### ARTICLE INFO

#### Keywords:

Crohn's disease  
Blood pressure variability  
Heart rate variability  
Autonomic function

### ABSTRACT

**Purpose:** The aim of the study was to assess cardiac and autonomic function in patients with Crohn's disease and explore their relation to disease duration using cardiovascular reflex tests.

**Materials and methods:** Cardiovascular parameters, baroreflex sensitivity, spectral-indices of short-term heart rate variability and blood pressure variability were compared between patients with Crohn's disease in remission (n = 30) and a control group (n = 29). Cardiac autonomic function was assessed during response to standing (tilt) and deep breathing test (expiration/inspiration ratio-E/I). Aortic pulse wave velocity, aortic augmentation index and central systolic blood pressure were measured oscillometrically.

**Results:** At rest, Crohn's disease patients had significantly higher systolic (p = 0.03) and diastolic (p = 0.03) blood pressure, total peripheral resistance index (p = 0.003), sympathetic-parasympathetic ratio (p = 0.033) and lower baroreceptor effectiveness (p = 0.047), myocardial variables (stroke index; p = 0.03, cardiac index; p = 0.025, Heather index; p = 0.039, left ventricular ejection time; p = 0.038), as compared to controls. Orthostatic response to the tilt test in the Crohn's disease group and the control group was similar, no intergroup differences were observed for E/I ratio and autonomic parameters. In Crohn's disease patients, disease duration was negatively associated with baroreflex sensitivity and positively correlated with normalised high frequency heart rate variability, sympathetic-parasympathetic ratio at rest and post-tilt changes in  $\Delta$ systolic blood pressure, p < 0.05. The control group had significantly lower central systolic blood pressure (p = 0.043) compared to Crohn's disease patients.

**Conclusions:** Crohn's disease patients in remission have preserved cardiac and autonomic function in response to cardiovascular reflex tests with a shift in cardiovascular autonomic regulation towards sympathetic predominate in the rest position.

### 1. Introduction

Both, Crohn's disease (CD) and ulcerative colitis (UC) belong to the group of inflammatory bowel diseases (IBD) that are characterised by their chronic nature and complex, multi-factor etiopathogenesis that is still not fully understood [1,2]. In CD the inflammatory process affects specific segments, involving all layers of the intestinal wall, and may affect any part of the gastrointestinal tract (GI), from the mouth to the anus [3]. However, it remains unknown whether the presence of the inflammation in the enteric nervous system (ENS) is a factor contributing to CD etiopathogenesis, or occurring as a consequence of the

disease [4].

CD may be considered as a systemic disease, since extraintestinal manifestations may affect 21–41% of patients; however, many manifestations are present regardless of the disease activity [5,6]. Therefore, it is still not fully known whether the presence of autonomic dysfunction in IBD results from damage to the peripheral or central autonomic nervous system (ANS) [7]. Diagnostic criteria suggest that cardiovascular autonomic neuropathy may affect approximately 5% of IBD patients [8,9]. Inflammation in the ENS may alter cardiac function in CD patients. Results of studies using heart rate variability (HRV) to evaluate ANS dysfunction in CD and UC patients are inconsistent [10].

\* Corresponding author at: Department of Hygiene, Epidemiology and Ergonomy, Nicolaus Copernicus University in Torun, M. Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland.

E-mail address: [monikazawadka@poczta.onet.pl](mailto:monikazawadka@poczta.onet.pl) (M. Zawadka-Kunikowska).

<https://doi.org/10.1016/j.advms.2018.04.009>

Received 7 August 2017; Accepted 26 April 2018

1896-1126/ © 2018 Medical University of Białystok. Published by Elsevier B.V. All rights reserved.

Some studies indicate that the IBD course is associated with increased [11,12] or decreased [8,9] ANS activity. Conversely, other authors indicate that IBD patients do not differ from healthy subjects of similar age in terms of ANS function [13]. Studies suggest that subclinical autonomic neuropathy may be a factor in predicting an increased mortality rate in IBD [14]. Therefore, detecting cardiovascular autonomic dysfunction in IBD might help to properly direct the treatment at earlier stages of the disease.

The aim of the current study was to assess cardiac and autonomic function in CD patients and explore their relation to disease duration using standardized cardiovascular reflex tests

## 2. Materials and methods

### 2.1. Subjects

We included in the study 30 subjects with CD and 29 age-matched healthy controls. The CD group consisted of 10 women and 20 men, between 20 and 46 years of age, with disease duration of 0.5–17 years. The control group consisted of 25 women and 4 men, between 20 and 46 years of age. All the patients have been in clinical and endoscopic remission for the last 10–12 weeks (according to Crohn's Disease Activity Index – CDAI < 150 scores) [15] (Table 1). Exclusion criteria were: cardiac arrhythmias, ischaemic heart disease, hypertension, diabetes mellitus, cancer diseases and treatment with beta-blockers, anticholinergic, antiarrhythmic or depressants.

### 2.2. Ethics approval

The study protocol was approved by the Ethics Committee at Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in

**Table 1**  
Subjects characteristics.

	CD	Control
Number of subjects [n]	n = 30	n = 29
Age [years]	30.8 ± 7.4	32.5 ± 6.2
Sex		
Female/Men	10/20	25/4
BMI [kg/m <sup>2</sup> ]	23.2 ± 3.8	21.8 ± 3.6
Disease duration [years]	8.6 ± 5.0	–
CDAI	93.6 ± 36.7	–
CRP [mg/l]	6.84 ± 9.72	–
RBC [mln/μl]	4.80 ± 0.54	–
WBC [tys./μl]	7.63 ± 2.85	–
PLT [tys./μl]	275.63 ± 62.54	–
MPV [fl]	8.40 ± 1.60	–
HG [g/dl]	13.89 ± 1.40	–
MCH [pg]	29.05 ± 2.58	–
MCHC [g/dl]	33.59 ± 1.33	–
Location, n (%)		
Ileum	5 (17%)	–
Colon	6 (20%)	–
Ileocolic	19 (63%)	–
Behaviour		
Inflammatory	18 (64%)	–
Stenosing	4 (14%)	–
Penetrating	6 (21%)	–
Drug group		
Anti-inflammatory	22 (93%)	–
Immunosuppressives	14 (46.6%)	–
Steroids	3 (10%)	–
Ant-TNF/Adalimumab	22 (73.3%)	–

CDAI - Crohn's Disease Activity Index; BMI - body mass index, CRP - C-Reactive Protein; RBC - red blood cell count; WBC - white blood cell count; PLT - platelet count; MPV - mean platelet volume; HG - hemoglobin; MCHC - mean corpuscular hemoglobin concentration; MCH - mean corpuscular haemoglobin.

Torun (approval number: KB 251/2015). All subjects provided written informed consent.

### 2.3. Cardiac haemodynamic and autonomic regulation

All measurements were conducted in conditions meeting criteria for functional testing of the ANS [16,17]. All cardiac and autonomic regulations were recorded using a Task Force Monitor (TFM, CNSystem, Medizintechnik, Graz, Austria). Beat-to-beat systolic (sBP) and diastolic blood pressure (dBP) were measured by a vascular unloading technique which was compared automatically to the oscillometric blood pressure measured on the contralateral arm [18].

The ECG was used to evaluate the heart rate (HR), while the impedance cardiography was used to evaluate stroke volume (SV), stroke index (SI = SV/body surface), cardiac output (CO = SV × heart rate), cardiac index (CI = CO/body surface), total arterial compliance (TAC = SV/PP), thoracic fluid content (TFC), left ventricular ejection time (LVET), left ventricular work index (LVWI), index of contractility (IC) and the Heather index (HI) representing positive cardiac inotropy. The total peripheral resistance index (TPRI) was calculated according to Ohm's law: total peripheral resistance index = mean BP/cardiac index [19]. The autonomic nervous system function was evaluated by baroreceptor sensitivity using sequence method and the spectral analysis of the short-term heart rate (HRV) and blood pressure variability (BPV) applying an autoregressive methodology. TFM calculates total power spectral density (PSD) and three frequency bands: very low frequency (VLF, 0–0.05 Hz), low frequency (LF, 0.05–0.17 Hz) and high frequency (HF, 0.17–0.40 Hz). LF band refers to sympathetic modulation of sinoatrial node (SA) and vasomotor function, while HF band to parasympathetic modulation of cardiovascular activity.

The power density of each spectral component was calculated both in absolute and normalised values (PSD-RRI, LFnu-RRI, HFnu-RRI for HRV and PSD-sBP, LFnu-sBP, HFnu-sBP, PSD-dBP, LFnu-dBP, HFnu-dBP for sBPV and dBPV). Ratio between LF and HF bands (LF/HF ratio) for heart rate and blood pressure variability represents the sympathetic-parasympathetic balance. Baroreceptor sensitivity (BRS) was calculated using sequence method as the slope of the linear regression between beat-to-beat sBP values (mmHg). Baroreceptor effectiveness index (BEI) was calculated as the ratio of baroreceptor to the number of BP ramps during 10 min of supine rest [20].

### 2.4. Clinical cardiovascular reflex tests

#### 2.4.1. Deep breathing test (DBT)

The DBT test assesses parasympathetic vagal nerve function. During the test subjects were asked to breathe at the frequency of 6 breathings per minute in the supine position. The E/I ratio was calculated as the mean of the longest R-R interval during expiration divided by the mean of the shortest R-R interval during inspiration [21,22] E/I ratio of > 1.11 was considered normal.

#### 2.4.2. Tilt test

The protocol included 20 min of baseline rest in the supine position followed by 5 min 20 s of tilt test at 70°. During tilting, the parameters were recorded at 1 min 20 s (phase I), 3 min 20 s (phase II), and 5 min 20 s (phase III). Changes in the body position were made using a tilt table with a foot support and fastening straps at the knee, hip and chest levels.

### 2.5. Arterial function assessment

Complex arterial function (stiffness) was performed using an Arteriograph (Tensiomed). Using the cuff for blood pressure measurements, the aortic pulse wave velocity (PWVao), the augmentation index (Aix) and the central systolic blood pressure (SBPao) were measured oscillometrically, and showed a strong correlation with the invasively

Download English Version:

<https://daneshyari.com/en/article/8368199>

Download Persian Version:

<https://daneshyari.com/article/8368199>

[Daneshyari.com](https://daneshyari.com)