An analysis of the correlation of clinical, endoscopic and histological classifications in Crohn's disease

Łukasz Durko[1], Olga A. Stasikowska-Kanicka[2], Małgorzata Wagrowska-Danilewicz[3], Marian Danilewicz[2], Ewa I. Małecka-Panas[1]

[1]Department of Digestive Tract Diseases, Medical University of Lodz, Poland
[2]Department of Nephropathology, Medical University of Lodz, Poland
[3]Pathomorphology Department, Medical University of Lodz, Poland

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Address for correspondence: Łukasz Durko MD, PhD, Department of Digestive Tract Diseases, Medical University of Lodz, 22 Kopcińskiego St, 90-153 Lodz, Poland, phone: +48 609 497 949, e-mail: ldurko@poczta.onet.pl

Abstract

Introduction: The precise evaluation of Crohn's disease (CD) activity is difficult mainly due to the complex symptoms of the disease. Establishing correlations between the most widely used scales of CD clinical, endoscopic and histopathological activity might help to identify the most accurate scale in the assessment of the course of CD.

Aim: Comparison of the results of clinical, endoscopic and histological scales of CD activity, i.e. (Crohn's Disease Activity Index (CDAI) score, Montreal Classification, Crohn's Disease Endoscopic Index of Severity (CDEIS) and D'Haens classification).

Material and methods: A group of 62 patients with CD was examined. All individuals underwent medical interview and physical examination. All patients had colonoscopy, at which the extent of the disease was analysed according to Montreal Classification and intensity of mucosal lesion described by CDEIS scale. Biopsy samples were taken during colonoscopy. Crohn's disease activity was evaluated by clinical scales (Montreal Classification – A and B, CDAI), endoscopic scales (Montreal Classification – L, CDEIS) and histopathological classification by D'Haens.

Results: The results of histopathological activity scale of CD by D'Haens correlated only with the results of endoscopic classification CDEIS. The results of CDEIS correlated also with parameter B of Montreal Classification. The analysis of Montreal Classification parameters showed correlations between the age of disease onset (A) and localization of the disease (L). Additionally, correlation of parameter A (age of onset) and B (behaviour of the disease) of Montreal Classification was observed. The values of clinical CDAI scale correlated only with parameter B of Montreal Classification (behaviour of the disease).

Conclusions: There was a significant correlation between the histological (D'Haens) classification and endoscopic scale (CDEIS), but their results did not correlate with clinical scales. There was no consistent correlation between the clinical scales themselves however the correlations concerned only some parameters assessed, which may be the result of subjective clinicians evaluation of CD activity.

Introduction

Precise and consistent classification of Crohn's disease (CD) activity is difficult due to the diversity of symptoms and common disproportions between the clinical course of the disease and the intensity of endoscopic or histological lesions.

One of the most widely used clinical classifications of CD is the Crohn's Disease Activity Index (CDAI) designed by Best *et al.* in 1976 [1]. The index consists of eight factors, each scored after adjustment with a standardized factor: the number of liquid stools per week, abdominal pain (graded 0–3 on severity), general well being (0–4), the presence of complications (1 point each), taking antiperistalsis drugs, the presence of abdominal mass (0 – none, 2 – questionable, 5 – definite), haematocrit (female: 42, male 47) and the percentage deviation from standard weight. Interpreting the results, CDAI < 150 represents remission of CD, 150–220 represents low activity, 220–450 represents moderate activity and more than 450 points represents high activity of the disease.

Table I. Example of CDEIS grading in CD according to [4]

	Rectum	Sigmoid and descending colon	Transverse colon	Ascending colon	Ileum	Sum
Deep ulcerations (12 – present, 0 – none)	0	0	0	12	–	12 (sum 1)
Superficial ulcerations (6 – present, 0 – none)	6	6	6	6	–	24 (sum 2)
Surface involved by the disease (/10 cm)	4.7	4.2	3.7	5.6	–	18.2 (sum 3)
Surface covered by ulcerations (/10 cm)	0.6	0.5	0.4	0.9	–	2.4 (sum 4)
Sum 1 + 2 + 3 + 4						56.6 (sum A)
Number of examined segments (1–5)						4 (n)
Sum/*n*						14.15 (sum B)
Presence of strictures with ulcerations – 3, no strictures – 0						3 (sum C)
Presence of strictures without ulcerations – 3, no strictures – 0						0 (sum D)
Sum B + C + D						**17.15 CDEIS**

Another commonly used scale of CD intensity is Montreal Classification designed by agroup of experts at the World Congress of Gastroenterology in 2005 [2]. It consists of clinical and endoscopic components. For the evaluation of CD course the authors included the age of onset (A1 – before 16 years old, A2 – 17–40 years old and A3 – above 40 years old), localization of lesions (L1 – limited to small intestine, L2 – colon, L3 – small intestine and colon and L4 – upper gastrointestinal tract) and behaviour of the disease (B1 – no strictures or fistulas, B2 – presence of strictures, B3 – presence of fistulas or B3p – presence of perianal lesions). The data suggests that early onset of the disease (A1) corresponds to a more intensive course of the disease and higher risk of complications [3].

The most widely used scale for evaluation of endoscopic lesions in CD is Crohn's Disease Endoscopic Index Score (CDEIS) developed by agroup of experts in 1989 [4]. It depicts four types of mucosal abnormalities: superficial ulcerations, deep ulcerations, strictures without ulcerations and strictures with ulcerations. The presence of those lesions is noted in all segments of intestine evaluated by colonoscopy: rectum, sigmoid colon, transverse colon, ascending colon and ileum. Additionally, the surface of mucosa involved by the disease is evaluated by endoscopists who mark the intensity of lesions on a 10 cm scale for each examined segment. Anexample of establishing a CDEIS score is presented in Table I. Despite its complexity, this endoscopic index is very precise and consistent.

For histological evaluation of CD activity the scale designedin 1989by D'Haens *et al.* is often used [5]. The following parameters are evaluated: epithelial damage (0–2 points), architectural changes (0–2 points), infiltration of mononuclear cells in the lamina propria (0–2 points), infiltration of polymorphonuclear cells in the lamina propria (0–3 points), presence of polymorphonuclear cells in epithelium (0–3 points), presence of erosions and/or ulcers (0–1 points), presence of granulomas (0–1 points) and the number of biopsy specimens affected (0–3 points). The maximum score is 16 points.

Despite many efforts, the above clinical, endoscopic and histological scales are still not fully satisfactory for the precise description of CD activity. Moreover, their results do not always correlate with each other. Therefore, by comparing the results of the most commonly used indices of CD intensity we aim at choosing the most accurate and simple method of evaluating CD course.

Aim

We compare the results of the most commonly used clinical, endoscopic and histological scales of CD activity, i.e. CDAI score, Montreal Classification, CDEIS and D'Haens classification.

Material and methods

A group of 62 patients with CD (28 men, 34 women, mean age 41.2 years) who had never received anti-tumor necrosis factor-α (TNF-α) therapy was examined. All individuals underwent medical interview and physical examination. Study protocol included the age of patients, gender, duration of the disease, height, body weight, intensity of pain, number of loose stools per week, general wellbeing, presence of complications and taken medications. All patients had colonoscopy

at which the extent of the disease was analysed according to Montreal Classification and the intensity of mucosal lesion described by CDEIS scale. To exclude the presence of abnormalities in the upper gastrointestinal tract all individuals underwent gastroscopy. Biopsy samples were taken during endoscopic procedures as indicated. The paraffin embedded specimens were stained by haematoxylin and eosin. Histological activity of the disease was evaluated according to D'Haens scale. For statistical analysis the *U* Mann Whitney and Pearson's χ^2 tests were used.

The study was conducted in the Endoscopy Unit at the Department of Digestive Tract Diseases and at the Department of Nephropathology, Medical University of Lodz in the years 2007–2011. The project received the approval of the Bioethics Committee of the Medical University of Lodz (RNN/44/09/KE).

Results

Crohn's Disease Activity Index scale

The values of clinical CDAI scale correlated only with parameter B of Montreal Classification (behaviour of the disease) (Figure 1). In the group of patients with active CD (CDAI > 170 points), strictures (B2) and fistulas (B3) were present more frequently than solely luminal lesions (B1) – (B2 + B3 vs. B1: 57.2% vs. 42.8%, $p < 0.05$). Additionally, individuals with low activity of the disease (CDAI < 170 points) presented more often only luminal abnormalities (B1) rather than strictures (B2) and fistulas (B3) – (B1 vs. B2 + B3: 66.7% vs. 33.3%, $p < 0.05$).

No correlation was noted between CDAI scale results and other parameters of Montreal Classification (age of onset – A, localization – L), endoscopic classification CDEIS or histological D'Haens scale.

Montreal Classification

The analysis of Montreal Classification parameters showed significant correlations between the age of disease onset (A) and localization of the disease (L). The more extensive lesions (L3) were present more often in individuals in whom CD was diagnosed before 40 years of age (A1 + A2), in comparison to those in whom the disease started later (A3): 71.0% vs. 34.8%; $p < 0.05$ (Figure 2). Subsequently, the lesions limited to colon (L2) or distal ileum (L1) were noted more commonly in group A3 than A1 (respectively: 43.5% vs. 19.3%, $p < 0.05$; 21.7% vs. 9.7%, $p < 0.05$.

Additionally, significant correlation of parameters A (age of onset) and B (behaviour of the disease) of Montreal Classification was observed. In the group of patients with no fistulas or strictures (B1) there were more individuals who were diagnosed with CD after 16 years of age (A2 + A3) than those who were diagnosed with the disease earlier (A1): A2 + A3 vs. A1 – 60% vs. 40%, $p < 0.05$. Furthermore, there were more individuals who had CD detected before 16 years of age (A1) than those who were diagnosed later (A2 + A3) in the group of patients who had strictures and fistulas (B2 + B3) – A1 vs. A2 + A3 – 54.9% vs. 45.1%, $p < 0.01$ (Figure 3).

No correlation was observed between the behaviour of disease (B) and its localization (L) – $p > 0.05$.

Parameter B (behaviour) of Montreal Classification was consistent with the results of endoscopic scale CDEIS (Figure 4). In the group of patients who had strictures

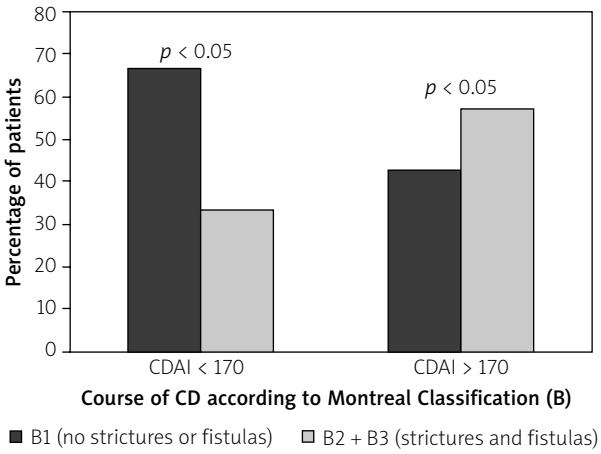

Figure 1. CD – Correlation of the results of Montreal Classification (Behaviour: B1 – no strictures, no fistulas, B2 – strictures, B3 – fistulas) and the results of CDAI index

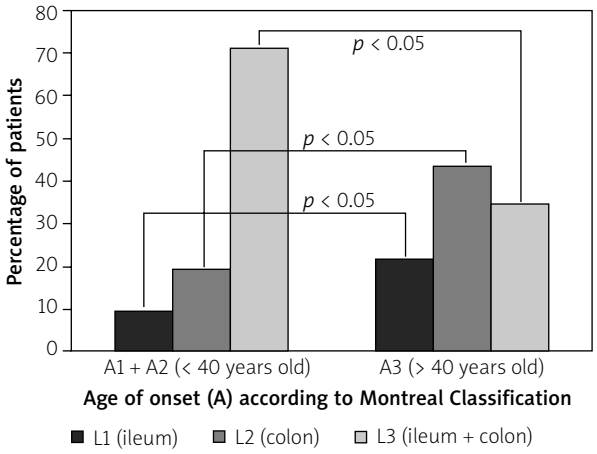

Figure 2. CD – Correlation of Montreal Classification results (age of onset A1 < 16 years of life, A2 16–40, A3 > 40 vs. localisation L1 – ileum, L2 – colon, L3 – ileum and colon)

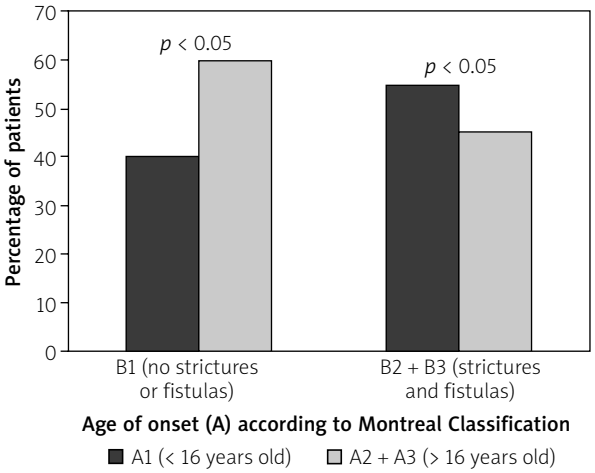

Figure 3. CD – Correlation of Montreal Classification results (age of onset A1 < 16 years of life, A2 16–40, A3 > 40 vs. behaviour B1 – no strictures, no fistulas, B2 – strictures, B3 – fistulas)

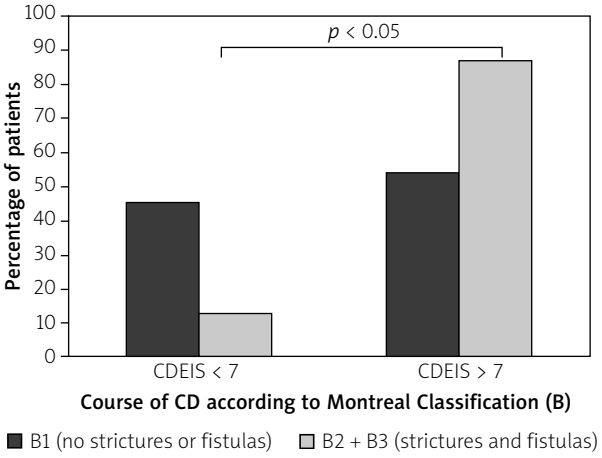

Figure 4. CD – Correlation of the results of Montreal Classification (Behaviour: B1 – no strictures, no fistulas, B2 – strictures, B3 – fistulas) and the results of endoscopic score CDEIS

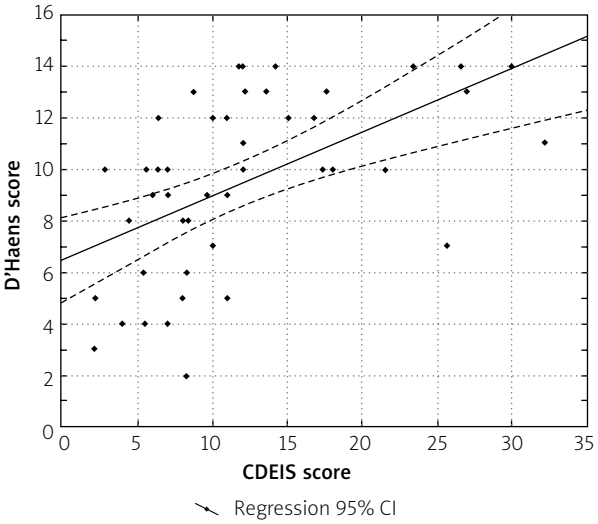

Figure 5. CD – Correlation of the results of endoscopic score CDEIS with the results of D'Haens histologic index ($p < 0.05$)

and fistulas (B2 + B3) intensive endoscopic lesions (CDEIS > 7) were present more often than subtle endoscopic abnormalities (CDEIS < 7) – (87% vs. 13%; $p < 0.05$).

The other parameters of Montreal Classification did not correlate with the endoscopic scale (CDEIS). Montreal Classification did not correlate with the results of D'Haens histopathological scale.

Crohn's Disease Endoscopic Index of Severity

The results of the endoscopic classification CDEIS correlated with the results of D'Haens histological scale ($r = 0.53$; $p < 0.05$) (Figure 5), and, as mentioned earlier, with parameter B of Montreal Classification (Figure 4). No correlation was observed between CDEIS results and other parameters of Montreal Classification and CDAI scale.

D'Haens Classification

The results of the histological classification correlated only with the results of the endoscopic scale (CDEIS) as mentioned earlier (Figure 5). There were no correlations of D'Haens score and other examined classifications.

The summarized results of the correlation of clinical, endoscopic and histological scales of CD are presented in Table II.

Discussion

Parameter B (behaviour) of Montreal Classification correlated with the CDAI score and corresponded also to parameter A (age of onset) of Montreal Classification. Additionally, parameter B correlated to the endoscopic score (CDEIS). However, it showed no correlation with D'Haens histological scale. Within Montreal Classification there was correlation between parameters A and L (localization) and also parameters A and B. No correlation was noted between parameters B and L. The endoscopic score (CDEIS) correlated with the results of D'Haens histological score and with parameter B of Montreal Classification.

The literature data on the correlations of particular parameters of Montreal Classification is limited. The International Working Party at the World Gastroenterology Congress in Montreal in 2005, who had designed this classification, did not consider it as fully precise in evaluating the activity of CD and in predicting the

Table II. Summarized results of clinical, endoscopic and histopathological scales correlation (Montreal Classification, CDAI, CDEIS and histopathological D'Haens) in CD

	Montreal Classification Parameter A (age of onset)	Montreal Classification Parameter B (behaviour)	Montreal Classification Parameter L (localisation)	CDAI	CDEIS	D'Haens histological activity
Montreal Classification Parameter A (age of onset)		+	+	–	–	–
Montreal Classification Parameter B (behaviour)	+		–	+	+	–
Montreal Classification Parameter L (localisation)	+	–		–	–	–
CDAI	–	+	–		–	–
CDEIS	–	+	–	–		+
D'Haens histological activity	–	–	–	–	+	

"+" – correlation present, "–" – no correlation

course of the disease. The authors assume that further understanding the pathogenesis of CD might lead to the improvement of classification quality, especially based on new genetic and serological tools [6].

However, the results of nationwide Crohn's disease registry in Poland showed that among patients who were diagnosed with the disease early (A1), lesions were mostly luminal (B1) – 70.32%, and their most common localization was ileocecal region (L3) – 67.8% [7].

In 1989 the Group of Experts (GETAID – Groupe D'Etudes Therapeutiques des Affections Inflammatoires du Tube Digestif) proposed the endoscopic CD scale CDEIS. The authors emphasized its value in grading endoscopic scores, but also showed its poor correlation with the CDAI scale (describing clinical symptoms and haematocrit value), which was explained by difficulties in comparison of clinical and endoscopic variables [8]. Similar results were presented in our study.

Laharie *et al.*, while investigating the role of methotrexate on mucosal healing in CD, evaluated the usefulness and correlations of different CD classifications. Contrary to our results, no correlation was found between CDEIS and D'Haens histological score. Those differences, however, might result from a lack of uniform specimen obtaining techniques from lesions at different localizations, inflammation intensity and, as a consequence, histological grading [9].

The data concerning correlations of CD clinical, endoscopic and histological classifications are scarce. Our results show that the results of Montreal Classification – parameter B (behaviour) correspond with the results of endoscopic index CDEIS and clinical CDAI index.

Additionally, the results of endoscopic CDEIS classification correlate with the results of D'Haens histological scale. This suggests the usefulness of those scales in evaluating CD activity.

The lack of uniform and corresponding scales of clinical, endoscopic and histological activity of CD confirms the complexity of the disease. The close correlation of endoscopic and histological scales suggests that the most objective method of evaluating CD activity is the evaluation of colonic mucosa.

Acknowledgments

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