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RĪGAS STRADIŅA UNIVERSITĀTE

Aleksejs Derovs

The Clinical Significance of the Excavated Lesions (Aphthae/Erosions, Ulcers) in the Small Bowel Detected by Capsule Endoscopy

Summary of the Dissertation
Specialty – Internal Medicine / Gastroenterology

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Dissertation was carried in Riga, Latvia on VSIA Paula Stradiņš clinical university hospital Gastroenterology centre and A/S Latvian Maritime Medicine Centre base.

Scientific supervisor:

Dr.med., asoc. professor **Juris Pokrotnieks**,
Riga Stradiņš University

Official reviewers:

Dr. habil. med., profesor **Aivars Lejnieks**,
Riga Stradiņš University

Dr. habil. med., profesor **Limas Kupčinskas**,
Lithuanian University of Health Sciences

Dr. med., asoc. profesor **Aldis Puķītis**,
Latvian University

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CONTENT

INTRODUCTION

Gastrotroenterology, as well as other fields of medicine, is constantly developing. In 2000, a fundamentally new method of endoscopy called video capsule endoscopy (CE) was introduced into clinical practice. CE entails the passive movement of a small medical device through the patient's gastrointestinal tract. The device records digital snapshots at regular intervals and sends those images via radio signals to a recording system. This new technology has proven to be particularly useful in patients with gastrointestinal bleeding of unclear aetiology, in those with anaemia and in patients with Crohn's disease. This diagnostic method is passive, less-invasive and well-tolerated by the patients [1].

CE is a new method in diagnostic endoscopy for the diagnosis of small bowel (SB) diseases. Due to this method, it is possible to assess the SB mucosa by differentiating intestinal villi and identifying the type of lesions. The basic lesion types are classified as flat [superficial] (e.g., maculas, laminas, angioectasias), protrusive (elevated) and excavated (aphthae/erosions, ulcers).

There is no data available in the literature, which shows the incidence of the excavated lesions in the small bowel farther than distal part of duodenum, in other words, farther than conventional endoscopical techniques possibilities allow. One of the frequent excavated lesion types in the upper (esophagus, stomach, proximal part of duodenum) or lower (colon) gastrointestinal tract are aphthae, erosions and ulcers. Clinical implication of the excavated lesions in the mentioned places is investigated and estimated very well. However, clinical implication of the excavated lesions in the small bowel is predominantly unknown. At this moment most data, which is related to the excavated lesions in the small bowel, is connected with bleeding and anemia, developing of strictures and risk of perforation. These data was obtained predominantly with "non-capsule" diagnostic modalities.

1. DESCRIPTION OF THE STUDY

1.1. Hypothesis

Clinical significance of the excavated lesions in the small bowel, which were ascertained by using a new diagnostic method - capsule endoscopy, should be similar to the clinical value of similar lesions in other regions of the gastrointestinal tract, ascertained by conventional endoscopic studies. In particular, taking into account the anatomical features of the small intestine, as well as the specific methods of the capsule endoscopy.

1.2. Aim of the study

To evaluate the clinical significance of the excavated lesions (aphthae/erosions and ulcers) diagnosed by capsule endoscopy in the small bowel.

1.3. Objectives

1. To evaluate demographic and vital signs (e.g. height, weight, body mass index, waist perimeter) of the patients, who underwent capsule endoscopy.

2. To gather major capsule endoscopy quality control parameters and to evaluate their impact on the diagnostic of the excavated lesions.

3. To estimate a possible association between patients anamnesis data and capsule endoscopy general parameters and the excavated lesions in the small bowel as well as indications for capsule endoscopy.

4. To estimate a possible association between Helicobacter pylori infection and the excavated lesions in the small bowel.

5. To estimate a possible clinical manifestations of the excavated lesions in the small bowel and association between other small bowel lesions and general laboratory findings (haemoglobin, white blood cells, erythrocyte sedimentation rate, C reactive protein).

6. To compare clinical implications of the excavated lesions in the small bowel diagnosed by capsule endoscopy with similar lesions in the other parts of gastrointestinal tract.

1.4. Scientific originality of the study

This study, for the first time is evaluating the relationship between the excavated lesions, diagnosed by capsule endoscopy, and patients' vital signs, diagnoses and other lesions of the small bowel. Furthermore, due to this study, it was possible to establish an incidence of the excavated lesions in major capsule endoscopy indications and those connections with Helicobacter pylori infection in the stomach.

Also, the impact of the quality control parameters on the capsule endoscopy was evaluated. This study is unique, because such research has not been published yet.

1.5. Working base and equipment

All the CE's were made either in VSIA Paula Stradiņš clinical university hospital or A/S Latvian Maritime Medicine Centre. Three CE systems were used: Olympus EndoCapsule (Japan), Given Imaging PillCam (Israel-USA), OMOM Capsule Endoscope (China). There was no statistically significant difference found in the literature between these systems. There was no preference for any specific capsule endoscopy system. Prior to CE examination, all patients had an upper and lower endoscopy and various radiological studies, including angiography, CT, MRI, irigoscopy and intestinal transit studies, with

no established pathology. Each patient completed a special questionnaire with 370 parameters that recorded the medical history of the patient, the results of performed laboratory and other studies and CE data, all of which were entered into the database.

1.6. Practical application

1. Work was done on the local Latvian patients and the resource base and demonstrates the clinical significance of capsule endoscopy in general and in connection with the excavated lesions in the small bowel in our region. Thus, respectively it is possible to change the patients' treatment plan.

2. Was obtained an approval for such controversial indication for CE as chronic abdominal pain.

3. We proved that erosions in the small bowel (erosive enteropathy) have certain clinical features, which are different from similar damage in the other parts of gastrointestinal tract.

4. We proved that the excavated lesions in the small bowel diagnosed by CE because of its anatomical difference (incomparably wider surface than in stomach or colon) are always with high clinical implication.

5. We established that patient's health status does not influence the transit time of capsule endoscope in the stomach and small intestine.

6. We used 3 from 4 commercially available CE systems and did not find any essential differences regarding to the safety profile or diagnostic yield.

7. In Latvia, as well as in the Baltics, only a small number of publications pertain to capsule endoscopy. The biggest experience in this field was obtained and specialized scientific and training centre was established.

1.7. The structure and size of work

Structure of the dissertation corresponds to the above formulated research objectives. Work is written in Latvian. It has 10 parts: Abstract in Latvian and English, introduction, description, literature review, materials and methods, results, result analysis and discussion, conclusions, references, list of the authors' publications and presentations, images and tables. The work has three attachments on 3 pages.

The size of the dissertation is 152 pages, bibliography consists of 176 references. The paper is 1 table and 117 images (out of these 52 authentic endofoto from the author's archive).

1.8. Conclusions from the literature review

1. Small bowel capsule endoscopy is a new investigational method in modern gastroenterology.

2. There is a lack of data regarding to the clinical value of capsule endoscopy.

3. The excavated lesions, clinical significance of which is very well investigated and estimated in the upper and lower gastrointestinal tract, practically was not investigated in the small bowel. Symptomatology of the lesions is also unknown. The relationship between those lesions and Helicobacter pylori infection still remains unclear.

4. Many different factors, such as quality control, the role of which due to the formation of excavated lesions has not been studied yet, can influence the outcome of capsule endoscopy and its clinical value. There are no publications related to capsule endoscopy In Latvia, as well as in the Baltic States

2. MATERIALS UN METHODS

2.1. Study design

Patients undergoing CE were prospectively studied. First 44 CE cases were not enrolled into the study to avoid bias results due to approbation of capsule endoscopy systems. These cases were used for construction of the database. There was no preference for any specific capsule endoscopy system and patient gender. Age restriction was applied to paediatric patients. Only those patients were enrolled in the study, which satisfied the inclusion criteria and were able to follow the instructions. Patients over 18 years of age signed informed consent. For patients younger than 18 years of age, the written informed consent was obtained from their parents.

The level of required care of the patients was assessed according to a scale developed by the Association of American Anaesthesiologists for evaluation of physical status of the patient. The term physical status proposed by the American Association of Anaesthesiologists was substituted by the term health status in our study [2]. Only the following first 4 categories from classification were applicable to our study:

- HS I – Normal healthy patient; localised pathological process is possible.
- HS II – Patient with mild systemic disease, such as 1 well-controlled illness.
- HS III – Patient with severe systemic disease, such as 2 or more mild, uncontrolled or poorly manageable diseases.
- HS IV – Patient with severe systemic disease that is a constant threat to life.

A complication was defined as any adverse event that changed the health status of the patient within 30 days after the CE.

2.2. CE procedure

The indications for CE diagnostics were consistent with the European Society of Gastrointestinal Endoscopy Guidelines [3-6]. We used three capsule endoscopy systems: Olympus Endocapsule, Given Imaging PillCam and OMOM Capsule Endoscope

These systems were equipped with their standard software applications. Pictures were taken at the rate of 2 fps. All patients underwent bowel preparation that consisted of either: a low-residue diet for 24 hours (in case if the polyethylene glycol-based electrolyte solution (PEG) was contraindicated) prior to CE; or the ingestion of 2 litres of PEG 24 hours prior to the examination (main scheme); or the ingestion of 4 litres of PEG 24 hours prior to the examination (if it was known, that the patient has delayed intestinal transit) [7-10].

2.3. *Helicobacter pylori* infection

All of the patients that were enrolled in the study were divided into two groups: H. pylori positive and H. pylori negative. Accurate determinations of H. pylori status were essential to the integrity of our study data. Therefore, H. pylori infection was established if two generally accepted diagnostic tests were positive: the rapid urease test during the upper endoscopy and a serologic test. [11,12].

2.4. Quality assessment

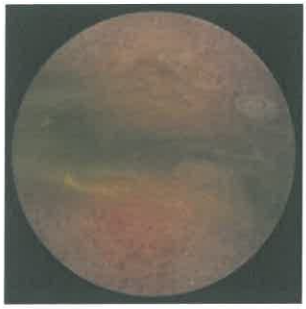
Three independent interpreters performed the analysis of each patient's CE recording. Internationally recognised definitions and criteria were used for these interpretations. The research was carried out in accordance with the

Helsinki Declaration [13]. This research was approved by the Local Ethical Committee.

2.5. CE diagnoses

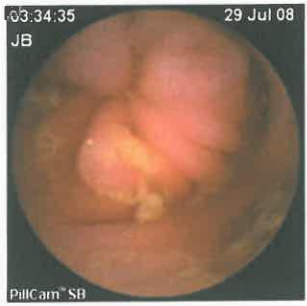
CE diagnoses were established in accordance with Capsule Endoscopy Standard Terminology (CEST) [14]. Enteropathy was defined as any disorder of the intestine. The following enteropathy classification was used in this study: erytematous, erosive, haemorrhagic, congestion, associated with the use of non-steroid anti-inflammatory drugs (NSAID) and celiac (gluten-sensitive).

NSAID enteropathy was established using the anamnesis (use of NSAID at least 6 months prior to CE) as well as diagnosing the visual changes in the small bowel mucosa (see *2.1. fig.*).



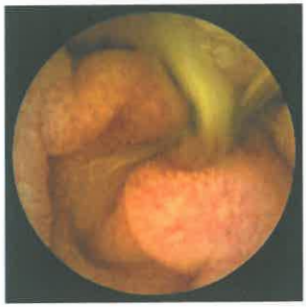
2.1. fig. NSAID enteropathy (Endofoto from the author's archive)

There was no publication found in the MEDLINE database to define erythematous enteropathy. With this term we defined a pathologic condition of the small bowel, which was characterized by redness of the mucosa and abnormal look of the villi (see *2.2. fig.*).



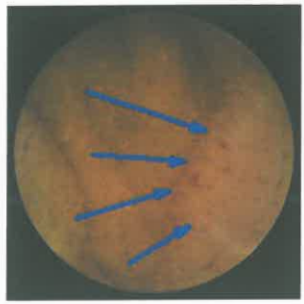
2.2. fig. Erythematous enteropathy (Endofoto from the author's archive)

There was no publication found in the MEDLINE database to define congestion enteropathy. With this term we defined a pathologic condition of the small bowel, which was characterized by plethora of the mucosa (swelling villi) and was outlined against a spastic bowel background (see *2.3. fig.*).



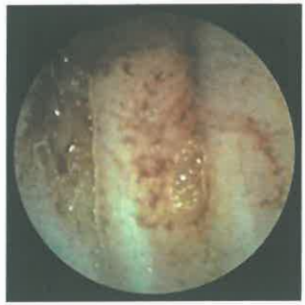
2.3. fig. Congestion enteropathy (Endofoto from the author's archive)

There was no publication found in the MEDLINE database to define erosive enteropathy. With this term we defined pathologic condition of the small bowel, which was characterized by visually diagnosed multiple various size erosions in each part of the small bowel (duodenum, jejunum, ileum) (see *2.4. fig.*).



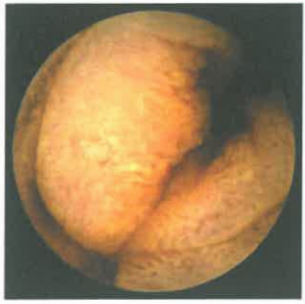
2.4. fig. Erosive enteropathy (Endofoto from the author's archive)

There was no publication found in the MEDLINE database to define haemorrhagic enteropathy. With this term we defined a pathologic condition of the small bowel, which was characterized by visually diagnosed multiple bleeding small bowel lesions. (sk. *2.5. fig.*).



2.5. fig. Haemorrhagic enteropathy (Endofoto from the author's archive)

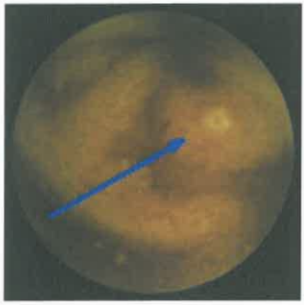
There was no publication found in the MEDLINE database to define segmental enteropathy. With this term we defined a pathologic condition of the small bowel, which was characterized by isolated damaged mucosal segments in the SB (see *2.6. fig.*).



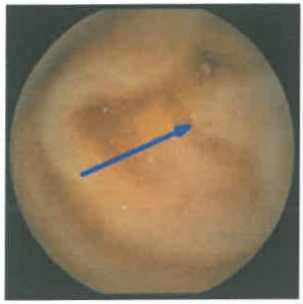
2.6. fig. Segmental enteropathy (Endofoto from the author's archive)

2.6. Excavated lesions

At the beginning of our trial, we used Minimal Standard Terminology Digestive Endoscopy, MST 2.0. According to MST 2.0, aphthae are defined as yellow or white spots that are surrounded by a red halo with a spot frequently in the centre. Erosion is defined as a small superficial defect in the mucosa with a white or yellow colour and a flat edge. However, according to the new version of Minimal Standard Terminology Digestive Endoscopy, MST 3.0, aphthae and erosions are consolidated into one group [15]. We marked the lesion as aphthae only if we were definitely sure about it (see *2.7. fig.*). Otherwise we marked the lesion as erosion. (see *2.8. fig.*). Ulcers are defined as mucosal breaks with white or yellow bases that are surrounded by red or pink collars..



2.7. fig. Aphthae (Endofoto from the author's archive)



2.8. fig. Erosion (Endofoto from the author's archive)

Only excavated lesions that extended diffusively in the SB were taken into account. Certain types of the excavated lesions were seen in all parts of the SB (e.g., duodenum, jejunum, ileum).

2.7. Small bowel cleansing level

The assessment of the small bowel cleanliness according to the scale we used was as follows: very good (no bubbles, no fluid in the lumen); satisfactory (bubbles and fluid are hindering visualisation); poor (due to the bubbles and fluid some areas cannot be visualised).

2.8. Regional transit abnormalities

During the CE, regional transit abnormalities (RTA) were evaluated. RTA interpretation was adopted from Tang and ICCE work group recommendation [16]. RTA was classified to one of the following types: 1. RTA1 – capsule is at least 60 min. in the definite segment without visual mucosal disorders; 2. RTA2 – capsule is at least 60 min. in the definite segment with visual mucosal disorders).

2.9. Statistical analysis

Database and statistical analysis were performed using SPSS ver.16. For this study different statistical methods (crosstabs, correlation coefficients etc.) were applied for statistical calculation. Only bivariate two-tailed correlation was used. Skewness and Kurtosis were used to check normal data distribution [17]. The following statistical methods and coefficients were used:

- Pearson chi-square was used to test the null hypothesis;
- Pearson correlation coefficient was used as a measure of the strength of linear dependence between two variables;
- Kendall's tau. Non-parametric tau test was used to measure the association between two measured quantities;
- Spearman's rho. Non-parametric test was used to measure statistical dependence between two variables. It assesses how well the relationship between two variables can be described using a monotonic function;
- Phi test was used as a measure of association for two binary variables;
- Somer's d. Somer's nonparametric d coefficient was used to measure the strength of association between two ordered scale variables;
- Goodman & Kruskal's lambda. Was used as a measure of proportional reduction in error in cross tabulation analysis.

In some cases several correlation coefficients were applied to check for significance and to avoid bias results. The impact of additional factors, including age, gender, body mass index, use of antibiotics and SB cleansing level etc., on the presence of the excavated lesions in the SB was evaluated using a non-parametric test. The Kruskal–Wallis one-way analysis of variance by ranks was applied for this purpose. The correlation coefficient distribution was as follows: $r = 0.8$ to 1.0 - a very strong correlation; $r = 0.5$ to 0.8 – average (tendency), $r = 0.2$ to 0.5 - weak correlation, less than 0.2 - negligible

correlation [18]. P-values are two-sided and were considered significant at the level of 5%.

3. RESULTS

3.1. Study patients general profile

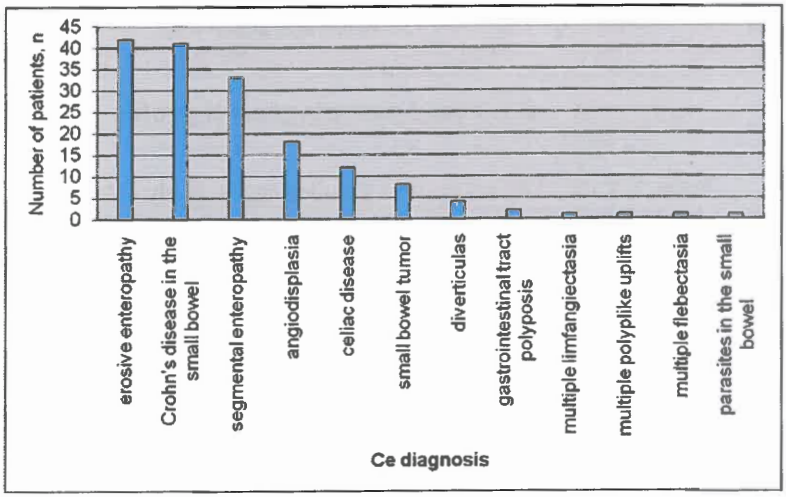
From 218 CE, 174 cases were enrolled in the study. The first 44 cases were excluded to avoid bias results, because of the approbation of the capsule endoscopy method. These cases were used to develop the study protocol.

Out of the 174 cases, 99 (56.9%) were females and 75 (43.1%) - males. There was no statistically significant difference between patients' gender in different study groups.

Patients' age ranged from 13 to 82 (44.99±17.63). Patients' height ranged from 150.0 to 198.0 cm (169.9±8.4). Patients' weight ranged from 28.0 to 114.0 kg (70.14±17.44). Patients' body mass index ranged from 12.44 to 39.45 (24.18±5.34). Patients' waist perimeter ranged from 52.0 to 120.0 (87.29±14.28).

The patients were referred for capsule endoscopy with the following diagnoses: suspected Crohn's disease - 60 (34.5%), obscure bleeding from gastrointestinal tract - 40 (23%), chronic anemia of unclear etiology - 25 (14.4%), chronic abdominal pain of unclear etiology - 25 (14.4%), celiac disease - 10 (5.7%), tumour in the SB - 10 (5.7%), suspected foreign body in the SB - 2 (1.1%), chronic diarrhea - 2 (1.1%).

Patients' distribution by CE diagnosis was as follows: erosive enteropathy - 42 (24.1%), Crohn's disease in SB - 41 (23.6%), segmental enteropathy - 33 (19.0%), angiodisplasia - 18 (10.3%), celiac disease - 12 (6,9%), tumour in the SB - 8 (4.6%), diverticulas in the SB - 4 (2.3%), SB polyposis - 2 (1.1%), multiple limfangiectasia - 1 (0.6%), multiple polyp-like mucosal uplifts - 1 (0.6%), multiple flebectasia - 1 (0.6%), parasites in the SB - 1 (0.6%) (see *3.1. fig.*)



3.1. fig. Patients' distribution by CE diagnosis

According to the health status (HS) the patients were divided into the following groups: HS I (n=44, 25.3%), HS II (n=51, 29.3%), HS III (n=76, 43.7%), HS IV (n=3, 1.7%). These assessments correlated to 54.6% of cases as having outpatient status (HS I and HS II) and 45.4% of cases as having an inpatient status (HS III and HS IV).

A total of 35 (20.1%) examinations were performed using the Given Imaging PillCam, 33 (19%) were conducted using the Olympus Endocapsule, and 106 (60.9%) exams were carried out with the OMOM Capsule Endoscope. No statistically reliable correlation between the 3 capsule endoscopy systems and the capsule transit time in the stomach or small bowel was found. All patients tolerated the examination well and did not complain of side effects. For each patient, at least 50,000 images (digital endophotography) were obtained. The data analysis conducted by each interpreter required approximately 1 hour and varied according to the pathology and the quality of bowel preparation. Capsule retention was observed in 2 patients with Crohn's disease.

Patients' distribution by bowel preparation scheme was as follows: 1) a low-residue diet for 24 hours – 20 (11.5%); 2) ingestion of 2 litres of PEG 24 hours prior to the examination - 145 (83.3%); 3) ingestion of 4 litres of PEG 24 hours prior to the examination - 9 (5.2%).

3.2. Patients' complains

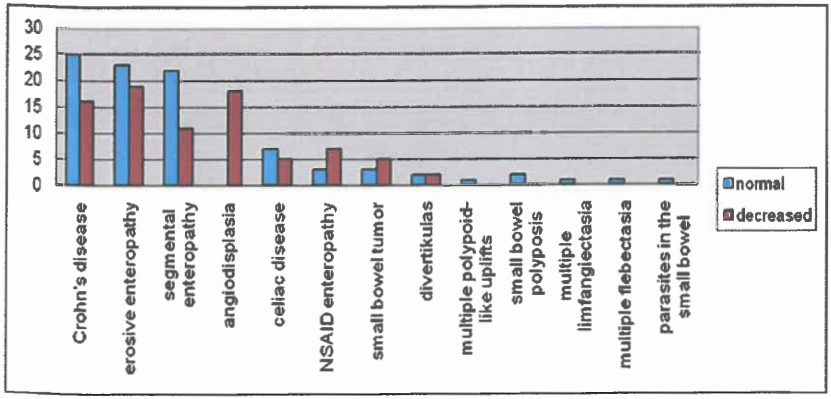
From 174 patients enrolled in the study, 120 (69%) had complains on fatigue, weakness and attrition. These complains prevailed in patients with following CE diagnoses: erosive enteropathy - 37 (30.8%), Crohn's disease - 24 (20,0%), angiodisplasia - 17 (14.2%), segmental enteropathy - 16 (13.3%). Statistically significant correlation was observed between patients' complains on fatigue, weakness and attrition and CE diagnosis ($\chi 2=28.883$; $p=0.004$).

From 174 patients enrolled in the study, 91 (52.3%) had complains on chronic abdominal pain. These complain prevailed in patients with following CE diagnoses: Crohn's disease - 27 (29.7%), erosive enteropathy - 23 (25.3%), segmental enteropathy - 16 (17.6%). Statistically significant correlation was observed between patients' complains on chronic abdominal pain and CE diagnosis ($\chi 2=23.370$; $p=0.025$). To be more precise, in certain CE diagnoses these complaints are more common than in others.

From 174 patients enrolled in the study, 29 (16,7%) had fresh blood in the stool. These complain prevailed in patients with following CE diagnoses: erosive enteropathy - 8 (27.6%), Crohn's disease - 7 (24.1%). However, no statistically significant correlation was observed.

3.3. Laboratory findings

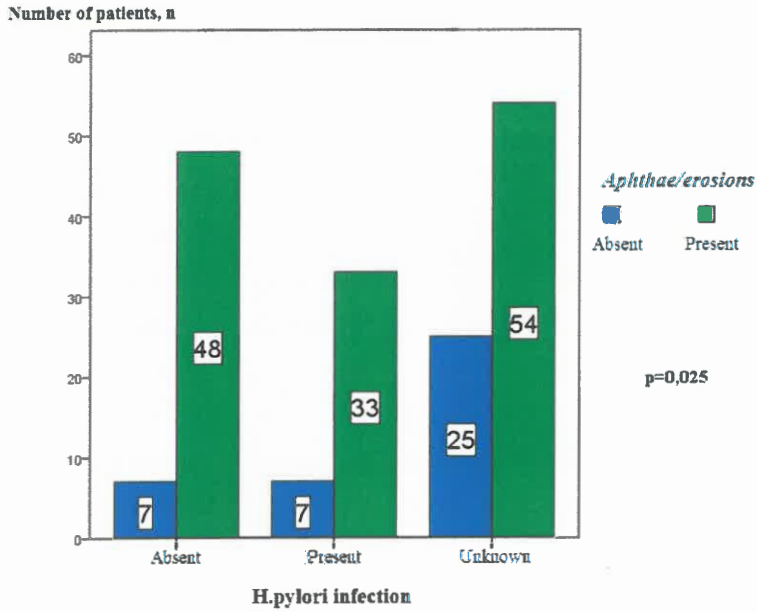
From laboratory findings, which were entered into the database, statistically significant connection was found only between decreased haemoglobin level and CE diagnosis ($\chi 2=32.157$; $p=0.001$) (see *3.2. fig.*).



3.2. fig. Distribution of haemoglobin level by CE diagnoses

Decreased haemoglobin level was established in 83 (47.7%) patients. Most frequently it was observed in patients with the following CE diagnoses: erosive enteropathy - 19 (22.9%), angiodisplasia - 18 (21.7%), Crohn's disease in the SB - 16 (19.3%), segmental enteropathy - 11 (13.3%) (fig. 16). Other laboratory findings (white blood cells, erythrocyte sedimentation rate, C reactive protein etc.) were statistically insignificant.

H.pylori infection prior to CE was established in 40 (23.0%) patients. H.pylori negative patients were 55 (31.6%) and in 79 (45.4%) patients diagnostic tests for this infectious agent were not performed. A positive statistically significant correlation was found between aphthae/erosions in the small bowel and H. pylori infection ($\chi 2=7.395$; $\phi=0.206$, probability $p=0.025$). It means that the incidence of aphthae/erosions in the SB is more frequent in patients with H.pylori infection (see *3.3. fig.*).



3.3. fig. *Helicobacter pylori* infection distribution by the presence of aphthae/erosions in the SB

3.4. CE general parameters

Total CE examination time was in a range from 309 till 631 min. (484.49±42.8). Stomach transit time was in a range from 2 to 441 min. (44.6±50.3). Small bowel transit time was in a range from 39 to 502 min. (279.35±89.66). In 25 (14.4%) cases capsule endoscope did not reach caecum. Mostly it was observed in patients with Crohn's disease 9 (36.0%), angiodisplasia - 5 (20.0%) and erosive enteropathy - 3 (12.0%). Furthermore, statistically significant correlation was observed between capsule endoscope small bowel transit time and CE diagnoses (r=0.111; probability p=0.042). It means that in certain CE diagnoses small bowel transit time was longer.

Regional transit abnormalities were observed in 31 (17.8%) patients. Mostly it was observed in patients with following diagnoses: Crohn's disease 14 (45.2%) and erosive enteropathy - 8 (25.8%). Statistically significant correlation was found between the existence of RTA and following parameters: 1) CE diagnoses (r=0.244; probability p=0.001); 2) blood in the bowel lumen ($\chi 2$=5.373; ϕ=0.176; probability p=0.02); 3) abnormal villi in the SB ($\chi 2$=6.919; ϕ=0.199; probability p=0.009); 4) negative correlation between angioectasia (r=-0,109; probability p=0.04); 5) ulcers in the SB ($\chi 2$=4.574; ϕ=0.162; probability p=0.033); 6) aphthae in the SB ($\chi 2$=5.517; ϕ=0.178; probability p=0.019).

Small bowel cleansing level according to our scale was as follows: perfect - 37 (21.3%), satisfactory - 123 (70.7%) and poor - 14 (8%).).

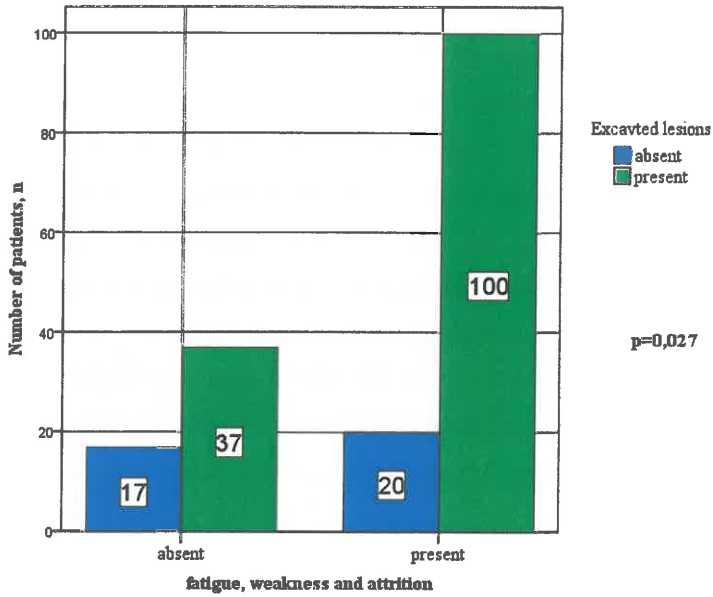
3.5. Excavated lesions

Excavated lesions were established in 137 (78.7%) patients. Out of these aphthae were observed in 15 (8,6%) patients, erosions - 133 (76.4%) and ulcers - 51 (29.3%). Moreover there were patients with simultaneously several types of excavated lesions (aphthae/erosions, ulcers) observed. Aphthae were observed mostly in patients with Crohn's disease - 7 (46.7%) and erosive enteropathy - 3 (20.0%). Erosions were observed mostly in patients with erosive enteropathy - 42 (31.6%), Crohn's disease - 35 (26.3%), segmental enteropathy - 19 (14.3%) and angiodisplasia - 11 (8.3%). Ulcers were observed mostly in patients with Crohn's disease - 19 (37.3%), erosive enteropathy - 10 (19.6%), NSAID enteropathy - 7 (13.7%) and angiodisplasia - 6 (11.8%).

Statistically significant correlation was found between:

• excavated lesions in the SB and patients complains on fatigue, weakness and attrition ($\chi 2$=4.882; ϕ=0.168; probability p=0.027). It means that

the excavated lesions are observed more often in patients with complains mentioned above (see *3.4. fig.*);



3.4. fig. Patients complains on fatigue, weakness and attrition distribution by the presence of the excavated lesions

• aphthae/erosions in the SB and H.pylori infection (ϕ=0.206; probability p=0.025). It means that the incidence of aphthae/erosions in the SB is more frequently observed in patients with H.pylori infection (see *3.3. fig.*);

• aphthae in the SB and RTA ($\chi 2$=5.517; ϕ=0.178; probability p=0.019). It means that RTA is more often observed in patients with aphthae in the SB;

• ulcers in the SB and RTA ($\chi 2$=4.574; ϕ=0.162; probability p=0.032). It means that RTA is more often observed in patients with ulcers in the SB;

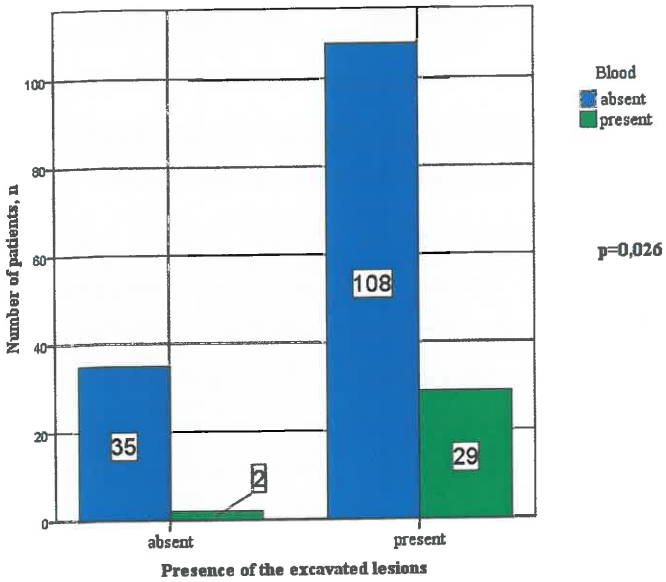
• ulcers in the SB and SB lumen changes (deformation, stricture, obstruction) ($\chi 2$=9.138; ϕ=0.229; probability p=0.003). It means that SB lumen changes are more often observed in patients with ulcers in the SB:

• ulcers in the SB and SB lumen stenosis ($\chi 2$=17.753; ϕ=0.319; probability p=0.000025). It means that SB lumen stenosis is more often observed in patients with ulcers in the SB;

• excavated lesions in the SB and SB lumen strictures (r=0.102; probability p=0.003). It means that SB lumen strictures are more often observed in patients with excavated lesions in the SB; (fig. 19)paveida;

• ulcers in the SB and SB fold regularity ($\chi 2$=5.449; ϕ=0.177; probability p=0.02). It means that in patients with ulcers in the SB, SB fold regularity is more rarely than in patients without ulcers

• excavated lesions in the SB and blood in the SB lumen ($\chi 2$=4.943; ϕ=0.169; probability p=0.026). It means that in patients with the excavated lesions blood in the lumen is much more common (see *3.5. fig.*);



3.5. fig. Blood in the SB lumen and the excavated lesions

• negative correlation between ulcers in the SB and bile in the SB lumen ($\chi 2$=9.582; ϕ=-0.235; probability p=0.002). It means that in patients with ulcers in the SB, bile in the bowel lumen is observed more rarely;

• excavated lesions in the SB and erythematous mucosa in the SB ($\chi 2$=5.399; ϕ=0.176; probability p=0.021). It means that in patients with the excavated lesions, erythematous mucosa is observed more frequently;

• aphthae in the SB and granular mucosa in the SB ($\chi 2$=17.092; ϕ=0.313; probability p=0.000036). It means that in patients with aphthae, granular mucosa is observed more frequently;

• ulcers in the SB and granular mucosa in the SB ($\chi 2$=4.472; ϕ=0.160; probability p=0.034). It means that in patients with ulcers, granular mucosa is observed more frequently;

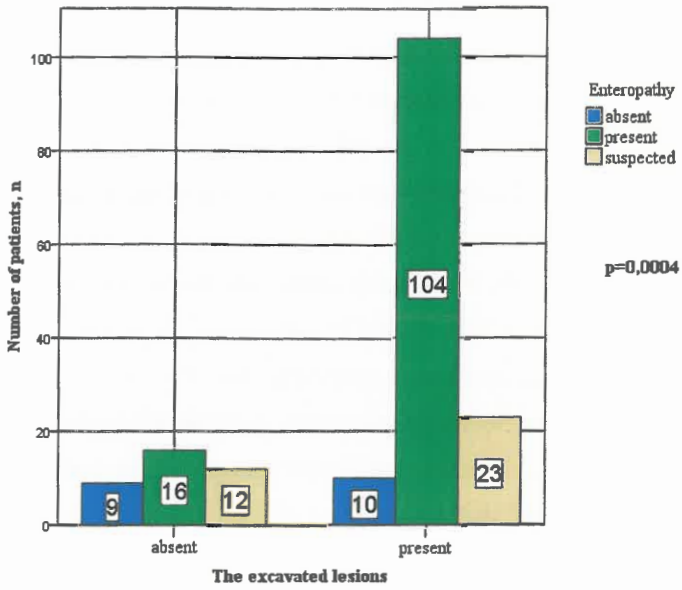
• aphthae in the SB and mosaic-like mucosa in the SB (r=0,110; probability p=0.048). It means that in patients with aphthae, mosaic reminiscent mucosa is observed more frequently;

• ulcers in the SB and celiac disease (r=0,034; probability p=0.01). It means that in patients with celiac disease, ulcers in the SB are observed more frequently;

• excavated lesions in the SB and Crohn's disease in the SB (r=0,167; probability p=0.046). It means that in patients with Crohn's disease in the SB, excavated lesions in the SB are observed more frequently;

• ulcers in the SB and NSAID enteropathy ($\chi 2$=11.826; ϕ=0.261; probability p=0.003). It means that in patients with NSAID enteropathy, ulcers in the SB are observed more frequently;

• excavated lesions in the SB and enteropathy diagnosis ($\chi 2$=15.786; ϕ=0.301; probability p=0.0004). It means that in patients with enteropathy diagnosis, excavated lesions in the SB are observed more frequently (see *3.6. fig.*);



3.6. att. Enteropathy and the excavated lesions in the SB

• ulcers in the SB and erythematous enteropathy (r=0,021; probability p=0.028). It means that in patients with erythematous enteropathy, ulcers in the SB are observed more frequently;

• excavated lesions in the SB and congestion enteropathy ($\chi 2$=5.991; ϕ=0.186; probability p=0.05). It means that in patients with congestion enteropathy, excavated lesions in the SB are observed more frequently;

• excavated lesions in the SB and haemorrhagic enteropathy (r=0.188; probability p=0.002). It means that in patients with haemorrhagic enteropathy, excavated lesions in the SB are observed more frequently;

• ulcers in the SB and bleeding from the SB ($\chi 2$=7.226; ϕ=0.204; probability p=0.007). It means that in patients with bleeding from the SB, ulcers in the SB are observed more frequently.

4. RESULT ANALYSIS AND DISCUSSION

A total number of 218 performed and 174 analysed CEs is a relatively small number. However, there is generally a small number of this type of examinations performed in other studies. At this moment we have the biggest experience in capsule endoscopy field in the Baltic States.

Patients' distribution by gender was homogeneous (56.9%/43.1%), wherewith patients' gender did not impact the results of the research. Patients' distribution by age, height, weight, body mass index or waist perimeter according to histogram with normal curve, skewness and kurtosis was also homogeneous.

Both adults and paediatric patients were enrolled in the study. It is well known, that CE is possible to perform not only in adults, but also in children [19,20]. Our experience, which was presented in 2009 on European Crohn's and Colitis Organisation congress, showed similar results [21]. One of the recent studies made by Jensen MK et al. was observed in 117 CE cases with different paediatric patients with Crohn's disease. The youngest was 10 months old. In his case capsule endoscope was placed into the duodenum with conventional endoscope. Authors of the study concluded, that in case of necessity CE could be performed for patients heavier than 11.5 kg. [23].

Chronic diarrhea is not included as an indication of the CE by Gastrointestinal Endoscopy Society (ESGE) guidelines. Several studies have been found in the literature regarding to this topic, with total number of patients to 200, describing chronic diarrhea, either in addition to symptoms of anemia, or as an independent indication for the CE [23-28].

4.1. CE diagnoses

Obtained results showed, that most frequent diagnoses in our study were enteropathy (erosive and segmental) and Crohn's disease in the SB. Comparatively rarely angiodisplasia, celiac disease, NSAID enteropathy and small bowel tumour were observed. These results give the evidence, that erosive and inflammatory lesions take up major of organic lesions in the SB diagnosed by CE. However, the results of the study have been definitely impacted by patients' selection for CE, to be more precise – by CE referral diagnosis.

4.2. Patients' health status

Capsule endoscopy for patients with an overall satisfactory health status (HS I or HS II) can usually be performed on an outpatient basis. Conversely, in patients with a more severe health condition (HS III or HS IV), this evaluation should be performed on an inpatient basis.

We conducted a literature review using the Medline database (for all years until December 2010) using the keywords "capsule endoscopy,", "transit time" and "physical status" or "health status". We did not find any data that assessed the relationship between patient health status and capsule endoscopy transit time. Nearly all manuscripts explored the potential correlation between transit time and the various patient preparation methods of liquids and other prokinetics. Two interesting articles described patients' characteristics and transit time. Papadopoulos AA and colleagues assessed the possible relationship between patient age and capsule endoscopy transit time in the stomach and small bowel in 120 patients [29]. They concluded that patient age does not correlate with transit time and does not influence how often the capsule reaches the caecum. However, they noted a trend among older patients

who were more likely to have angiodysplasia and an increased number of small bowel tumours. The authors suspected that this trend could be associated with the reduction of both lumen size and gut motility. Velayos JB and colleagues assessed the relationship between capsule endoscope transit time and patient age, gender, body mass index and waist size in 89 patients [30]. The authors concluded that CE transit time does not correlate with the aforementioned parameters.

The safety of capsule endoscopy in patients with severe disease is a very important factor, the positive solution of which would promote reception of useful information about the condition of the small bowel and possible pathologies.

The most common indication for CE is bleeding from the gastrointestinal tract with an unclear aetiology or anaemia. In these cases, capsule endoscopy is especially useful and effective. Until the invention of capsule endoscopy, the small bowel was the undiscovered area of the gastrointestinal tract. As a rule, such patients underwent a strict bed regimen, considerable dietary limitations and treatment with medicines that could negatively affect intestinal motility. Patient immobilisation led to a concern that capsule endoscopy transit time through the gastrointestinal tract would be increased. Therefore, a hypothesis developed among clinicians that capsule endoscopy would not reach the caecum within an 8 hour period and would therefore lead to incomplete examination of the small bowel.

Patients with Crohn's disease have lesions localised throughout the gastrointestinal tract. However, those lesions (70% of cases) are often found in the terminal ileum. In these patients, CE is indicated to evaluate the degree of small bowel involvement in the disease process, the pathology type and the spread of the disease to determinne treatment strategy. Among inpatients (HS III and HS IV), capsule endoscopy did not reach the caecum as often as it did in patients examined in outpatient setting (HS I and HS II). Therefore, our

hypothesis that patient disease severity would correlate with CE transit time was not confirmed. We consider CE to be a safe option in various patient groups with a range of diseases, irrespective of the patient's health status [31].

The incomplete examination of the small bowel that occurred in some cases was not considered to be a complication, but rather a characteristic of the exam dependent on many factors, including some that are uncontrollable. Based on literature data, the capsule endoscope reaches the caecum in 85% of cases [5,32,33]. Our results confirmed a similar rate (85.6%). Based on the results, the cases with incomplete examination had no statistically significant correlation with the diagnoses, including Crohn's disease. Still, our research offers further evidence that CE is a safe and well-tolerated method to examine the small bowel, including those of severely ill patients (HS III and HS IV) who are immobilised and at the hospital.

4.3. Capsule endoscopy system

We employed 3 capsule endoscopy systems, the Olympus endocapsule, the Given Imaging PillCam and the OMOM Capsule Endoscope, along with their corresponding software programs. Capsule endoscopy systems are similar in nature and primarily differ according to the placement of electrodes on the patient's body and the software program used. Major part of the CE was made with the OMOM Capsule Endoscope. This fact could possibly influence our results. However, we did not find a statistically significant correlation among those 3 capsule endoscopy systems used and the transit time to the stomach or the small bowel, in spite of the fact that the OMOM capsule is slightly larger in size and heavier. Furthermore, all these systems are accepted in the world, having appropriate certificates. In our research there was no preference for the certain system selection. According to that our previous experience, which was presented on World Congress of Gastroenterology / United European

Gastroenterology Week in 2009 [34, 35], shows, that there is no statistically significant difference between these three systems. It should be taken into account, that CE system selection is usually based on economical and organisational points neither on research and medical ones. We have proved that we were able to equally well master and use any commercially available CE.

4.4. Patients' complains

Fatigue, weakness and attrition. Due to our results, major part of the patients – 69% - had complains on fatigue, weakness and attrition. Out of these 37 (31%) patients had erosive enteropathy, 24 (20%) – Crohn's disease in the SB and 16 (13%) – segmental enteropathy. It is known, that one of the inflammatory bowel diseases symptoms are fatigue, weakness and attrition. However, its linkage with erosive and segmental enteropathy has not been described. Erosive enteropathy is mostly described as solitary erosive lesions either in the upper part of duodenum or in terminal ileum in case of Crohn's disease. Furthermore, such lesions are often associated with the use of NSAID. Our data shows, that erosive and segmental enteropathy have often statistically significant correlation with the above mentioned complains, because of its high incidence in case of erosive enteropathy (88%) from all the cases of erosive enteropathy and 49% from all cases of segmental enteropathy.

Chronic abdominal pain. Half of the patients (91, 52%) had complains on chronic abdominal pain of unknown origin. Out of these 27 (30%) had Crohn's disease, 23 (25%) – erosive enteropathy and 16 (18%) – segmental enteropathy. In case of inflammatory bowel diseases, chronic abdominal pain is a common symptom. However, it has not been previously related to the existence of erosive or segmental enteropathy. Our results show that both erosive and segmental enteropathy often correlate with the patients' complains

on abdominal pain. The above mentioned complains are observed in 55% of patients with erosive enteropathy and 49% - segmental enteropathy. This is highly important, because it shows that patients with chronic abdominal pain of unknown origin having other diagnostical procedures with negative results should undergo capsule endoscopy. Wherewith, we can consider that the above mentioned symptom is an important indication for CE.

Fresh blood in the faeces. According to our data, fresh blood in the feaces prior to CE was observed in 29 (17%) of the study group. Out of these in 8 (20%) of patients was diagnosed erosive enteropathy and in 7 (17%) – Crohn's disease in the SB. It is known, that in case of Crohn's disease, fresh blood in the faeces is one of the major symptoms. Every fifth patients from our study with erosive enteropathy had direct bleeding signs (fresh blood in stool). Consequently, erosive enteropathy is a potential cause of rectal bleeding. .

4.5. Laboratory

From all laboratory parameters, which has been analysed in this study, we found statistically significant correlation only between decreased level of haemoglobin and CE diagnosis (probability p=0.001). Decreased level of haemoglobin was established in 83 (47.7%) of patients prior to CE. These results show that the anaemia's symptom is one of the most frequent symptoms in patients referred to CE. Due to the literature data, one of the most frequent causes of bleeding from gastrointestinal tract and accordingly cause of anemia are angiodsiplasia (vascular malformations) and Crohn's disease in the SB. According to our results, most frequent causes of anaemia were erosive enteropathy (22.9%), followed by angiodsiplasia (21.7%) and Crohn's disease in the SB (19.3%). It is worth mentioning, that the visual outlook of the pathologies mentioned above is different and this fact in its turn minimizes the occurrence of the false interpretation. The finding of erosive enteropathy has an

important clinical implication because it was proven, that erosions in the SB (even without inflammatory bowel disease) are the cause of anaemia, probably because of periodical bleeding. Other frequent cause of anemia according to our research was segmental enteropathy. We have proven that segmental enteropathy causes anaemia relatively frequently. It can be explained due to villi. To be more precise, inflamed areas change the absorption abilities (due to inflammation and oedema) of the villi and iron cannot be assimilated by the SB even if the patient is assuming plenty enough of iron with food. This finding allows putting the decreased level of haemoglobin to one of the additional criteria for CE indications.

4.6. *Helicobacter pylori* infection

Despite the fact that H. pylori is the main cause of deep excavated lesions (ulcers) in the stomach, we did not find a significant correlation between H. pylori infection and ulcers in SB. However, the correlation (probability p=0.025) between aphthae/erosions and this infectious agent was established. One possible explanation for this result could be the small number of patients enrolled in our study, because superficial excavated lesions, such as aphthae/erosions, are much more common pathology in SB than ulcers. Therefore, to evaluate the correlation between deep excavated lesions and H. pylori infection, we may need to enlarge the number of patients that contained ulcers in the SB. We also did not find any statistically significant impact of additional factors, such as age, gender, body mass index, use of NSAIDs and antibiotics, Crohn's disease or small bowel cleanliness level, on the existence of excavated lesions in the SB. However, the influence of other pathologies (synergy) that were not assessed in the study on excavated lesion development in the small intestine cannot be excluded.

A MEDLINE database search up to May 2010 using the English keywords capsule endoscopy, Helicobacter pylori, excavated lesion/defect, aphthae, ulcer and erosion, produced no studies that assessed the correlation between H. pylori infection and excavated lesions in the SB as diagnosed by CE. Predominantly, all of the previous studies of H. pylori have focused on the oesophagus, stomach and duodenum. These studies showed that the presence of H. pylori influences the development of excavated lesions in these anatomic regions. H. pylori is the most common factor that causes stomach (60-80% cases) and duodenal (70-90% cases) ulcers [11,36]. This infectious agent reduces the protective mucous layer that defends the wall of the stomach and duodenum from the destructive action of the gastric acid. H. pylori invasion only occurs in the stomach, which has a very acidic environment (pH=1.2-2). However, these bacteria also cause injuries in the duodenum where pH level is 7-8. Because the duodenum is a proximal part of the small intestine, it was logical to hypothesise that these bacteria could also influence the development of excavated lesions in the jejunum and ileum because H. pylori reduces the protective barrier of the small intestine. Therefore, the wall of the intestine becomes more sensitive to irritations or changes in the pH, which promotes the development of excavated lesions.

There are various publications in the literature that point to an association of H. pylori with small intestinal diseases. In her literature review of the possible association between H. pylori and celiac disease, Szaflarska-Poplawska concluded that there is a correlation between the presence of H. pylori and celiac disease [37]. However, all of the patients with established celiac disease were free of H. pylori infection in our study. This result suggests that the role of this infectious agent in excavating lesions remains controversial. Unfortunately, most previous studies have been heterogeneous and of modest quality. In a study performed by Sullivan PB et al. in 1990 that included 294 paediatric patients of different ages and 119 people in the control group, an

association between H. pylori and chronic diarrhoea and malnutrition was shown [39]. In 2000, Yon Ho Choe et al. published an article that analysed the association of H. pylori with iron deficiency anaemia and the retarded growth of children during puberty. More than 500 children were included in this study. The authors concluded that the combination of these two factors, the presence of H. pylori infection and iron deficiency anaemia, significantly delayed the growth of the child during the puberty.

The hypothesis that H. pylori was associated with excavated lesions in the small intestine was partly proven with a statistically significant correlation in our study. A correlation between H. pylori and aphthae/erosions in the SB was found ($p=0.025$). Interestingly, the role of H. pylori, which is the main infectious agent that causes damage (ulcers) in the stomach, has not been shown in the SB ($p=0.826$). A possible explanation for this result is the relatively small number of patients with ulcers in the SB in our study. However, these results are very important because they show a direction that further studies should investigate. The clinical impact of H. pylori infection should be reconsidered. If H. pylori infection in the stomach influences the lesions in the small intestine and causes erosions and enteropathies, then the possible influence of this pathological process would be supported. Therefore, it would be necessary to eradicate H. pylori in the unaffected upper gastrointestinal tract without pathological mucosal changes but with superficial excavated lesions in the small intestine. It is also possible to hypothesise that this infectious agent influences the development of small intestinal tumours and inflammatory bowel diseases, which could change the generally accepted diagnostic and therapy guidelines. However, more double-blinded randomised studies must be performed to reach a consensus on this issue.

4.7. Excavated lesions

At the beginning of our trial, we used Minimal Standard Terminology Digestive Endoscopy, MST 2.0. However, according to the new version of Minimal Standard Terminology Digestive Endoscopy, MST 3.0, aphthae and erosions are consolidated into one group (please refer to material and methods).

It is interesting, that in literature, scientists quite often do not follow this classification, as a result it is possible to encounter with such terms as aphtoid ulcer etc. This situation shows that MST classification is not perfect, as in praxis during both conventional and capsule endoscopy it is not possible to distinguish one lesion type from another. Wherewith, in our study, we labelled excavated lesion as aphthae only in cases when we were absolutely sure. If it was not possible to distinguish aphthae from erosion, we followed by MST 3.0 classification. To be more precise, we interpreted such lesion as erosion [15].

According to our research results, excavated lesions were one of the most frequent (78.7%) lesion types in the SB. Similarly to other parts of gastrointestinal tract, from all the types of excavated lesions most frequent ones – 133 (76.4%) were erosions (superficial lesions of the SB mucosa). Comparatively rarely – 51 (29.3%) ulcers were observed. Finally, the rarest – 15 (8.6%) - excavated lesion types were aphthae.

Our results show that excavated lesions in the SB are connected with patients' complains on weakness, fatigue and attrition (probability $p=0.028$). It means that in patients with the above mentioned complains, excavated lesions are diagnosed much more frequently.

A MEDLINE database search (keywords: small intestine, excavated lesions, weakness, attrition, fatigue) did not show any results. According to our data, excavated lesions were found in 83.3% of patients with the above mentioned complains. This fact points out clinical significance of excavated lesions in the SB and could be additional criteria for CE indication.

Excavated lesions in the SB correlate with blood in the bowel lumen (probability p=0.026). It means that in patients with diagnosed excavated lesions in the SB, blood in the bowel lumen is diagnosed more frequently, respectively 21.2% against 5.4%. It shows that the excavated lesions in the SB are one of the causes for bleeding. It is worth mentioning, that not only ulcers are potential generally accepted source of bleeding. Our data shows statistically accurate results, that erosions/aphthae could be a source of bleeding as well. That is why it is highly important to start appropriate treatment of patient in case of diagnosed erosions/aphthae in the SB, to prevent bleeding and further anaemisation. In case of such findings in stomach and proximal part of duodenum, all the above mentioned is on principle absolutely different from the treatment tactic. Wherewith, excavated lesions in the SB have an important clinical implication, which has not been estimated previously.

A MEDLINE database search (keywords: small intestine, erythematous mucosa, excavated lesion) did not show any results. However, according to our results the positive statistically significant correlation between the presence of excavated lesions in the SB and erythematous mucosa was observed. It means that in patients with erythematous SB mucosa, excavated lesions are encountered more often. Clinical implication of this finding is controversial.

A MEDLINE database search (keywords: small intestine, congestion enteropathy, excavated lesion) did not show any results. Our data by establishing statistically significant correlation (probability p=0.05) between excavated lesions in the SB and congestion enteropathy allows to evaluate clinical implication of this type of enteropathy. This result can be explained by the following speculation. In case of congestion enteropathy, blood flow of the SB mucosa is decreased; this is followed by secondary ischemia. To be more precise, temporary blood flow disorder occurs. As a result, protective layer of

the SB mucosa becomes feebler and defects of the mucosa appear. This leads to excavated lesions emergence.

A MEDLINE database search (keywords: small intestine, haemorrhagic enteropathy, excavated lesion) did not show any results. However, our results showed statistically significant correlation (probability p=0.002) between excavated lesions in the SB and haemorrhagic enteropathy. This fact allows evaluating this connection as clinically important. Though, at this moment we do not have a logical explanation of this association.

All the above mentioned, explains statistically significant correlation (probability p=0.0004) between excavated lesions in the SB and enteropathy diagnosis. It means that in patients with any type of enteropathy excavated lesions in the SB are more common. Therefore, any kind of enteropathy is an increased risk for the emergence of excavated lesions in the SB. It is known, that Crohn's disease manifestation in the SB is associated with excavated lesions at this area, especially with ulcers and their complications. Wherewith, our results have proven this fact.

Erosions, as it was expected, most frequently were associated with idiopatic erosive enteropathy – 42 (31.6%), Crohn's disease – 35 (26.3%), segmental enteropathy – 19 (14.3%) and angiodisplasia – 11 (8.3%). There is a lack of information regarding to erosive enteropathy in the literature. In case of the SB, they are mostly mentioned as solitary erosive lesions in case of different pathological conditions (Crohn's disease in the SB, other autoimmune lesions, NSAID enteropathy etc.). This means, that clinical implication of such diagnosis (erosive enteropathy) has not been evaluated. It is interesting, that despite of relatively good described erosive lesions in case of Crohn's disease (as one of the most frequent etiologic factors of these lesions), our results showed that it is not the first frequent cause, but the second. Besides, there were no marks, signs or suspicion of inflammatory bowel disease in patients with erosive enteropathy. This fact testifies that erosive enteropathy could be

idiopatic and more double-blinded randomised studies must be performed to reach a consensus on this issue.

In case of segmental enteropathy and angiodisplasia, multiple erosions in the SB were found conformably in 14.3% and 8.3% cases. Our results allow concluding that segmental enteropathy is erosion developing risk. Hypothetically, it can be presumed, that segmental enteropathy is the forerunner of erosive enteropathy. Wherewith, it is important to evaluate the necessity of treatment in case of segmental enteropathy.

According to our data, aphthae were often observed in patients with Crohn's disease instead of patients with erosive enteropathy. Then aphthae indicate more probability of Crohn's enteritis. However, combining aphthae and erosions into one group, as it was proposed by MST 3.0 classification, we are losing this option. Wherewith, automatic usage of MST 3.0 enteroscopic classification decreases the diagnostic value.

It is interesting, that we have found statistically significant correlation between aphthae and ulcers in the SB and RTA, conformably $p=0.019$ and $p=0.032$. This means that RTA is more frequently observed in patients either with aphthae or ulcers in the SB. It can be explained by the speculation that RTA is the forerunner of congestion enteropathy. Wherewith, in case of transit abnormalities the bowel spasm occurs, which is preceding temporary blood flow disorders. As a result, protective layer of the SB mucosa becomes feebler and defects of the mucosa appear. This leads to development of excavated lesions. However, progressing RTA, congestion enteropathy expands, which in its turn deteriorates the SB mucosal condition.

Explicitly positive statistically significant correlation was found (probability $p=0.000036$) between aphthae and granular mucosa in the SB. It means that in patients with granular mucosa aphthae in the SB are observed more often. According to literature, aphthae in the SB mostly is associated either with Crohn's disease in the SB or celiac disease. Connection with

infection (Yersinia enterocolitica, lambliasis) is also mentioned [39-42]. However, we did not found any data on granular mucosa and its potential connection with aphthae. We can hypothesize, that granular mucosa is primary manifestation of autoimmune disorder.

According to our results, ulcers in the SB were most frequently found in patients with Crohn's disease – 19 (37.3%), erosive enteropathy – 10 (19.6%), NSAID enteropathy – 7 (13.7%) and angiodisplasia – 6 (11.8%). It is known that one of the most frequent manifestations of Crohn's disease in the SB are ulcers. Our research results confirm this data. A MEDLINE database search (keywords: small intestine, erosive enteropathy, ulcer) did not show any results. However, the fact that erosive enteropathy was the second frequent cause of ulcers gives evidence for high clinical implication of this diagnosis. Tight statistically significant correlation showed the connection between ulcers in the SB and celiac disease (probability $p=0.01$) and NSAID enteropathy (probability $p=0.003$). It means that in patients with the diagnoses mentioned above, ulcers are observed much frequently. It is known, that one of the celiac disease complications is ulcerative jejunoileitis [40]. Consequently our study results concur with the literature data. In case of long-lasting use of NSAID, complication development from these drugs is possible. One of the NSAID enteropathy manifestations are ulcers. It can be solitary or multiple and varies from tiny to huge circular. From all of our cases ulcerative NSAID enteropathy was comparatively common diagnosis. Clinicians should take such fact into account.

Statistically significant negative correlation (probability $p=0.002$) was found between ulcers in the SB and bile in the SB lumen. It means that in patients with diagnosed ulcers in the SB bile in the bowel lumen was visualized rarely. It is known that bile in the esophagus or stomach is a pathological condition. However, our results show that bile in the bowel lumen is beneficial factor. We can speculate that bile has a protective impact on the SB mucosa.

Statistically significant positive correlation was found between ulcers in the SB and SB lumen changes (deformation, stricture or obstruction). This fact confirms a well-known thesis, that ulcers have dangerous complications, respectively distort and/or reduce the SB lumen. This situation can promote the development of ileus. Very tight positive correlation (probability p=0.00003) was found between ulcers in the SB and SB bowel luminal stenosis. This fact confirms high clinical implication of ulcers.

Statistically significant connection was found between ulcers in the SB and SB fold architectonics. We have observed that in patients with such lesions regular layout of the SB fold is rare. Taking into account this fact, we can assume that ulcers in the SB are not only the cause of organic disorders, but also the functional ones. If the folds in the SB become chaotic, then nutrition drive through the SB is frustrated. Furthermore, such situation can lead to malabsorption and develop clinical signs such as flatulence or even abdominal pain. However, more double-blinded randomised studies must be performed to reach a consensus on this issue.

Obtained results show the connection between ulcers in the SB and erythematous enteropathy (probability p=0.028). It means that in patients with erythematous enteropathy ulcers are observed more often. Thereby, we can speculate, that erythematous enteropathy is ulcer developing risk in the SB.

Statistically significant positive correlation (p=0.008) was found between ulcers in the SB and bleeding from the SB. It means that in patients with ulcers, bleeding from the SB was observed more often. According to literature data [32], most frequent causes of the SB bleeding are angiodisplasia, ulcers and carcinoma. Furthermore it could be ulcer of any aetiology (Crohn's disease, NSAID enteropathy etc.). It proves that such excavated lesions as ulcers have as high clinical implication in the SB as in the other parts of gastrointestinal tract.

MEDLINE database search (keywords: small intestine, excavated lesions, clinical implication) did not show any results. Our research shows and reveals new regularities between the SB lesions, clinical manifestations and laboratory findings.

Taking into account the fact that in the literature there is a lack of data regarding to similar studies in the field of excavated lesions in the SB, we had to compare these lesions with similar ones in the other parts of gastrointestinal tract (esophagus, stomach, proximal part of the duodenum, colon), where its clinical implication is incomparably better and longer studied. Thereby it is better known.

5. CONCLUSIONS

1. There is no statistically significant correlation between CE patients' demographic and physical data (height, weight, body mass index, waist perimeter) and the excavated lesions in the small bowel.

2. Quality control parameters overall satisfied CE methodology and did not significantly impact on the study results.

3. Excavated lesions in the SB are statistically significantly connected with patients' complains on fatigue, weakness, attrition. In this case sending the patient to the CE should be considered.

4. Aphthae/erosions are frequently found in patients with H.pylori infection.

5. Decreased level of haemoglobin is statistically significantly connected with capsule endoscopy diagnosis.

6. Excavated lesions in the small bowel diagnosed by CE because of its anatomical difference (incomparably wider surface than in stomach or colon) are always with high clinical implication. Even in case of superficial (erosive) lesions occupying insignificant part of the bowel (segmental enteropathy).

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