

# Pit pattern analysis using acetic-acid magnification chromoendoscopy in predicting histopathology of small colorectal polyps. The diagnostic yield and intra-/inter-observer reproducibility

Ocena wzoru ujść krypt jelitowych podczas chromoendoskopii przy użyciu kwasu octowego z powiększeniem obrazu w przewidywaniu histopatologii małych polipów jelita grubego. Zysk diagnostyczny i powtarzalność obserwacji

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**Key words:** endoscopy, chromoendoscopy, colonoscopy, magnification endoscopy, acetic acid, gastrointestinal polyps.

**Słowa kluczowe:** endoskopia, chromoendoskopia, kolonoskopia, endoskopia z powiększeniem obrazu, kwas octowy, polipy przewodu pokarmowego

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## Abstract

**Aim:** The purpose of the study was to assess the diagnostic yield of acetic-acid magnification chromoendoscopy and Kudo's classification of pit patterns in predicting neoplastic histopathology of small colorectal polyps, and to assess intra- and inter-observer reproducibility in classifying small colorectal polyps to particular pit patterns.

**Material and methods:** The prospective study was performed on 40 consecutive patients referred for non-therapeutic colonoscopy in whom 50 polyps with a diameter of less than 10 mm were found (endoscope Olympus CF Q160Z). An acetic acid solution (1.5%) and Kudo's pit pattern classification were used. All polyps were removed and examined histopathologically. The pit pattern was judged by an endoscopist immediately after colonoscopy. Then, anonymized digital video recordings of magnification colonoscopies were secondarily evaluated after 4 weeks (intra-observer reproducibility) by 2 other endoscopists. Inter-observer reproducibility was assessed using video recordings by 3 endoscopists comparing judgements of pit patterns (3 pairs of comparisons).

**Results:** Fifty polyps were evaluated: 25 hyperplastic, 18 adenomas, 6 with normal mucosa and 1 adenocarcinoma. During magnification colonoscopy 30 polyps were judged as non-neoplastic (pit pattern I and II in 5 and 25 cases, respectively) and 20 polyps were classified as a neoplastic pit pattern (III L and IV in 18 and 2 cases, respectively). Sensitivity and

## Streszczenie

**Cel:** Celem głównym badania było określenie zysku diagnostycznego chromoendoskopii z powiększeniem obrazu przy użyciu kwasu octowego oraz klasyfikacji wzoru ujść krypt jelitowych wg Kudo w przewidywaniu wyniku badania histopatologicznego małych polipów jelita grubego i odbytnicy. Kolejnym celem było określenie powtarzalności powyższej oceny u jednego badającego endoskopisty i między różnymi badającymi.

**Materiał i metody:** Badaniem prospektywnym objęto 40 kolejnych chorych skierowanych do diagnostycznej kolonoskopii, u których stwierdzano polipy wielkości poniżej 10 mm (50 polipów). Podczas endoskopii z powiększeniem obrazu (kolonoskop Olympus CF Q160Z) użyto 1,5-procentowego roztworu kwasu octowego i klasyfikacji Kudo w analizie wzoru ujść krypt jelitowych. Wszystkie polipy po usunięciu zostały zbada- ne histopatologicznie. Endoskopista wykonujący kolonosko- pię ocenił wzór ujść krypt jelitowych bezpośrednio po bada- niu. Anonimowe nagrania wideo ponownie ocenione przez tego samego badacza po 4 tyg. (powtarzalność oceny u tego samego badającego) oraz dodatkowo niezależnie przez 2 in- nych doświadczonych endoskopistów. Powtarzalność oceny u różnych badających ustalono przez porównanie 3 ocen en- doskopistów (3 pary porównań).

**Wyniki:** Oceniono 50 polipów: 25 hiperplastycznych, 18 gru- czolaków, 6 z prawidłową śluzówką i 1 gruczolakoraka. Pod- czas kolonoskopii z powiększeniem obrazu 30 polipów ocenio-

specificity of the pit pattern analysis in predicting neoplastic histopathology were 63.2 and 74.2%, respectively. Intra-observer reproducibility in classifying polyps to non-neoplastic and neoplastic pit patterns was very good ( $\kappa$  value 0.88). K values for assessment of inter-observer (three pairs of observers) reproducibility were 0.71, 0.38 and 0.32.

**Conclusions:** Acetic-acid magnification endoscopy is of a limited value in predicting neoplastic histopathology of small colorectal polyps with acceptable intra-observer reproducibility and unsatisfactory inter-observer reproducibility.

## Introduction

Acetic-acid magnification chromoendoscopy gains significance in gastrointestinal endoscopy. Cellular mechanisms allowing acetic acid to be used in chromoendoscopy have been recognized [1]. Studies concerning its usefulness in detection of intestinal metaplasia, dysplasia and early cancer in Barrett's esophagus [2-6] as well as early gastric carcinoma [6] have been published. Acetic acid was also proposed as a support in magnification chromoendoscopy to judge small colorectal polyps [7, 8].

Pit pattern analysis can be implemented in differential diagnosis between non-neoplastic and neoplastic colorectal lesions [9, 10]. The classification of pit patterns described by Kudo [10] distinguishes 6 types of pit patterns: I (typical of normal colonic mucosa), II (attributable to hyperplastic polyps in most cases) and types III (L and S), IV and V (usually neoplastic lesions).

Studies dealing with the use of the acetic acid in colonoscopy are scarce [7, 8]. Intra-observer and inter-observer reproducibility in classifying small colorectal polyps to particular pit patterns by acetic-acid magnification chromoendoscopy have not been established.

## Aim

The aim of the study was to analyse the use of acetic-acid magnification chromoendoscopy in prospective analysis of pit patterns of small colorectal polyps. The particular aims were to assess (1) the diagnostic yield of acetic-acid chromoendoscopy and Kudo's classification of pit patterns in predicting neoplastic histopathology of small colorectal polyps and (2) intra- and inter-observer reproducibility in classifying small colorectal polyps to non-neoplastic and neoplastic pit patterns.

no jako nienowotworowe (typ I wzoru ujęć krypt – 5 polipów, typ II wzoru ujęć krypt – 25 polipów), natomiast 20 polipom przypisano nowotworowe wzory ujęć krypt jelitowych (typ III L – 18 polipów, typ IV – 2 polipy). Czułość i swoistość oceny wzoru ujęć krypt jelitowych w przewidywaniu nowotworowego charakteru małych polipów jelita grubego wyniosły odpowiednio 63,2 i 74,2%. Powtarzalność oceny u konkretnego badającego była bardzo dobra (współczynnik  $\kappa$  0,88). W ocenie powtarzalności między różnymi badającymi wartości współczynnika  $\kappa$  wyniosły w poszczególnych parach: 0,71, 0,38, 0,32.

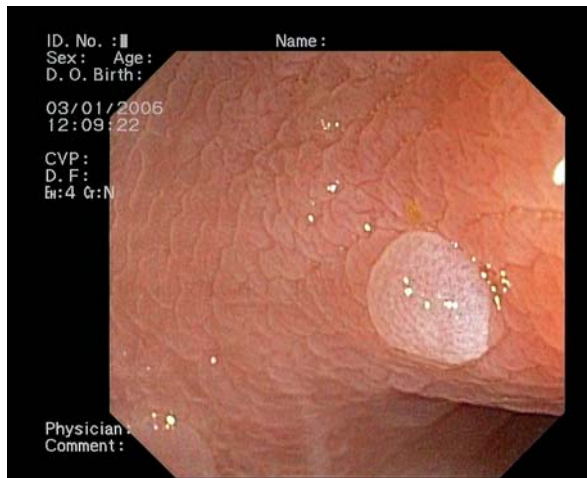
**Wnioski:** Kolonoskopia z powiększeniem obrazu i przy użyciu kwasu octowego ma ograniczoną wartość w przewidywaniu nowotworowego charakteru małych polipów jelita grubego. Powtarzalność oceny u konkretnego badającego jest dobra, podczas gdy powtarzalność oceny między różnymi badającymi jest niezadowalająca.

## Material and methods

This prospective study was carried out during one month (February 2006) in the endoscopy unit that is a part of the tertiary referral centre for gastrointestinal diseases. The unit works on the basis of an open access system. Every endoscopist participating in this study performed about 200 procedures with magnifying colonoscopy before the study. A single gastroenterologist (M.K.) with a 15-year experience in colonoscopy and 2-year experience in magnification chromoendoscopy performed all colonoscopies. Possible contraindications were evaluated in every patient. The performance of the examination did not infringe the safety of patients in any aspect.

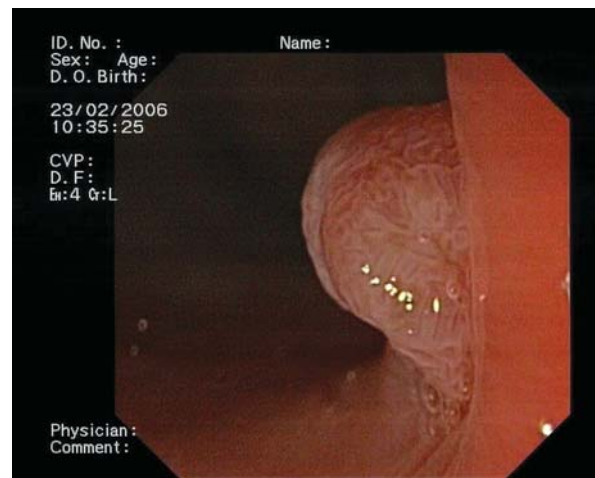
The study was performed on patients referred for diagnostic endoscopy, in whom at least one polyp of less than 1 cm was found. The patients referred for therapeutic or urgent endoscopy and those with no colorectal polyps were not included in the study. Patients with a history of inflammatory bowel disease, hereditary nonpolyposis colorectal cancer, familial adenomatous polyposis, with a history of previous colonoscopy or referred for surveillance endoscopy were not included to the study.

At the first stage of the study, colonoscopy was performed. Three to four litres of a polyethylene glycol solution was used for bowel preparation. Standard sedoanalgesia (with propofol or a combination of pentanyl, midazolam and short-acting barbiturates) was used. Sedation with monitoring (ECG, pulsoximetry) was done by an anesthesiologist. Magnification colonoscope CF Q160Z (Olympus Corp., Tokyo, Japan) with magnification controller Olympus MAJ-570 (Olympus Corp., Tokyo, Japan) were used. Videoendoscopy processor Olympus EXERA CV 160 (Olympus Corp., Tokyo, Japan) and monitor Olympus OEV 203 (Olympus Corp., Tokyo, Japan) were also used. At this stage, the patients



**Fig. 1.** Picture after acetic acid spraying and magnification of a polyp with pit pattern II, histopathologically – hyperplastic polyp

**Ryc. 1.** Obraz polipa z typem II wzoru ujść krypt po zastosowaniu kwasu octowego i powiększenia obrazu – w ocenie histopatologicznej polip hiperplastyczny



**Fig. 2.** Picture after acetic acid spraying and magnification of a polyp with pit pattern III L, histopathologically – tubular adenoma with low grade dysplasia

**Ryc. 2.** Obraz polipa z typem III L wzoru ujść krypt po zastosowaniu kwasu octowego i powiększenia obrazu – w ocenie histopatologicznej gruczolak cewkowy z dysplazją małego stopnia

in whom colonoscopy revealed lesions attributable to the inflammatory bowel disease, polyposis syndrome and/or colorectal cancer were excluded.

At the second stage, acetic acid magnification chromoendoscopy was performed in patients with at least 1 colorectal polyp with a diameter of no more than 1 cm. The diameter and localization of the lesion were recorded. An open biopsy forceps technique was used to establish the size of the polyp. A solution (1.5%) of acetic acid of approximately 10 ml (5-15 ml), using a syringe with a cushion of air, was spread over the area of the polyp through the working channel of the colonoscope. The polyp was later inspected under the magnification of 50-150 $\times$  (Figures 1, 2) and its pit pattern according to Kudo's classification was defined as non-neoplastic (I and II) or neoplastic (III L, III S, IV, and V) [10]. Pit patterns were judged in real time. Frozen images of each polyp were recorded for further evaluations. The images were stored as bit maps of approx. 1 MB each, resolution: 96 dpi vertically and 96 dpi horizontally, 720  $\times$  576 pixels, 24-bit color). The films (compression Dvmax codec, approx. 40-50 MB, sequence duration 10-15 s, 25 pictures/s, 24-bit color, 720  $\times$  576 pixels). The original images were transmitted using the standard protocol: digital imaging and communication in medicine (DICOM) to the server that hosted the database. Recording EndoRAAD interface (a module of NetRAAD), software provided by the University Health Care (UHC), Lublin, Poland, was used.

Each polyp was removed either by snare polypectomy or a cold biopsy technique. Specimens were fixed in 4% buffered formalin, processed routinely and stained with hematoxylin and eosin. The histopathologist was not aware of the pit pattern classification of polyps.

At the third stage, the recordings which were digitally stored on the hard disc were anonymized. They were evaluated and attributed to the type of pit patterns by the same endoscopist 4 weeks later. The same recordings were also evaluated by two independent endoscopists (H.B., G.R.). Every endoscopist was blinded for pit pattern judgement proposed by the other. Recordings were not changed and/or graphically modified in any way.

Four pit pattern judgments were established for each polyp: one – judged during the first examination in real time, second – four weeks later by the same endoscopist on the basis of anonymized recordings for intra-observer reproducibility and the next two judgements – established on the basis of recordings – by two independent endoscopists. Inter-observer reproducibility was assessed using video recordings by 3 endoscopists comparing judgements of pit patterns (3 pairs of comparisons). For simplicity, pit patterns were classified into 2 groups – non-neoplastic (I, II) vs. neoplastic (III L, III S, IV, V). The results of the histopathologic examination were categorized to neoplastic polyps (adenomas, adenocarcinomas) and

**Table I.** Demographics and clinical characteristics of the studied group**Tabela I.** Charakterystyka demograficzna i kliniczna badanej grupy

Feature		
Number of patients	40	
Male: female ratio	10 : 30	
Mean age ( $\pm$ SD)	52 ( $\pm$ 9)	
Number of removed polyps	50	
Indications for colonoscopy	Iron-deficiency anaemia	5
	Rectal bleeding	8
	Uncomplicated lower abdominal pain	10
	Change in bowel habits (pred. constipation)	7
	Uncomplicated diarrhoea	5
	Miscellaneous (e.g. lesion of recent barium enema, fecal occult blood test positive, unexplained weight loss)	5
Exclusion criteria	History of IBD, polyposis syndromes	
	Previous colonoscopy (with/without polypectomy)	
	Surveillance colonoscopy	

non-neoplastic polyps (hyperplastic polyps, polyps with normal mucosa).

Assessment of the diagnostic yield of the pit pattern in predicting neoplastic histopathology consisted in the relation between pit patterns conformed to neoplastic and non-neoplastic lesion (evaluated as a diagnostic test) and the result of the histopathologic examination (considered as the gold standard). Sensitivity, specificity, positive (PPV) and negative (NPV) predictive value, and diagnostic accuracy (correct classification rate) of diagnoses of neoplastic pit patterns in predicting neoplastic histopathology of colorectal polyps were calculated.

For assessing intra-observer reproducibility, the percentage of agreement and  $\kappa$  coefficient (and 95% of confidence intervals) for pit patterns (non-neoplastic vs. neoplastic) evaluated twice by the same endoscopist (during the colonoscopy and later using the recording) was calculated. Similarly, for assessing inter-observer reproducibility, the percentage of agreement and  $\kappa$  coefficients (and 95% of confidence intervals) for 3 pairs of comparisons for pit patterns (recordings evaluated by three endoscopists) were calculated.

Before investigation, the informed consent for acetic-acid magnification chromocolonoscopy was obtained from each patient. During collection, analysis and interpretation of data, the patients were provided with full anonymity. The examination was performed in conformity with guidelines of the Helsinki Declaration, after written permission was obtained from every examined person.

## Results

Demographic data and characteristics of patients are given in Table I. All patients were referred for colonoscopy

due to symptoms compatible with clinical scenarios described by the European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE, [www.epage.ch](http://www.epage.ch)). More precisely, the patients fulfilled criteria described as scenarios 8-12 and 18. Clinical scenario number 8 is iron-deficiency anemia (malabsorption syndrome excluded); clinical scenario number 9 is hematochezia (without inflammatory bowel disease – IBD; clinical scenario number 10 is uncomplicated lower abdominal pain of at least 2 months' duration, without known IBD, anemia or FOBT-positive stools; clinical scenario number 11 is change in bowel habits (predominantly constipation) of at least 2 months' duration without pain, known IBD, anemia or FOBT-positive stools; clinical scenario number 12 is uncomplicated diarrhoea after exclusion of infectious or malabsorption aetiology and without known IBD, no anemia or bleeding and not referred for colorectal cancer screening; clinical scenario number 18 comprises miscellaneous indications like a lesion at recent barium enema or sigmoidoscopy, FOBT-positive stools, fulminant colitis, endometriosis and unexplained weight loss [11-14]. None of the examined patients showed contraindications for colonoscopy, there were no inconclusive colonoscopies and no complications, either.

**Table II.** Inter-observer reproducibility**Tabela II.** Powtarzalność obserwacji u różnych badających

Pair of observers	Correct classification rates	K value
1	86% (95% CI 73-94)	0.71 (95% CI 0.5-0.9)
2	70% (95% CI 55-82)	0.38 (95% CI 0.1-0.6)
3	68% (95% CI 53-80)	0.32 (95% CI 0.1-0.5)

Sixteen polyps were localized in rectum, 24 in the sigmoid colon, 3 in the ascending colon, 4 in the transverse colon and 3 in the descending colon. Pit pattern judgement performed in real time (during chromocolonoscopy) revealed 5 polyps with pit pattern I, 25 polyps presented pattern II (Figure 1), 18 polyps – pattern III L (Figure 2) and 2 polyps – pattern IV. Pit patterns III S and V were not encountered. At histopathology, 19 polyps were found to be neoplastic (18 adenomas, 1 adenocarcinoma) and 31 polyps were non-neoplastic (25 hyperplastic and 6 with normal mucosa). Sensitivity, specificity, PPV, NPV and diagnostic accuracy of pit patterns in prediction of neoplastic histopathology of small colorectal polyps were: 63.2% (95% CI 38-84), 74.2% (95% CI 55-88), 60% (95% CI 36-81), 76.7% (95% CI 58-90) and 70% (95% CI 55-82), respectively. Intra-observer reproducibility in classifying polyps to non-neoplastic and neoplastic based on pit patterns was very good [correct classification rate 94% (95% CI 83-99),  $\kappa$  value 0.88 (95% CI 0.7-1.0)]. The results of the assessment of inter-observer reproducibility are collected in Table II.

## Discussion

The implementation of acetic acid in gastrointestinal endoscopy was promising because the agent is cheap, safe and easily accessible [2, 4, 5, 7, 8]. Besides, the use of acetic acid is rapid and reversible, hence potentially repeatable [2, 5, 8]. In this study we confirm that the technique is easy to use and not associated with side effects. Acetic-acid chromoendoscopy can be used for differentiation of neoplastic and non-neoplastic polyps, thus superfluous polypectomy can be avoided [7].

Togashi *et al.* [7] reported that the acetic acid is very efficient in highlighting pit patterns, which allows predicting with high accuracy histopathology of small colorectal polyps. In the presented study, the diagnostic yield of the pit pattern analysis in predicting neoplastic histopathology of small colorectal polyps using acetic-acid magnification chromoendoscopy was unsatisfactory. Our results are clearly inferior to the results of Togashi *et al.* [7] and are not as good as in indigo-carmin enhanced magnification endoscopy [15, 16]. The source of such different results could be technical aspects as magnifying chromoendoscopy with acetic acid is an operator-dependent method [3, 5].

Fortun *et al.* [4] pointed out that the pit pattern analysis by acetic-acid magnification endoscopy is characterized in the diagnosis of intestinal metaplasia, dysplasia or early cancer in Barrett's esophagus by a moderate to substantial level of inter- and intra-observer disagreement, however, in other studies there was a high variability of these parameters [17, 18]. Huang

*et al.* [9] demonstrated that inter- and intra-observer agreements in the judgement of the colonic pit pattern in indigo carmine chromocolonoscopy were remarkable, with mean  $\kappa$  values exceeding 0.7 and 0.8, respectively. However, the authors admit that the endoscopic prediction of histopathological diagnoses based on pit pattern analyses is complex and 'somewhat artificial'. In the study by Kiesslich *et al.* [19] inter-observer variation in the judgement of pit patterns during indigo carmine magnification chromocolonoscopy did not exceed 50%. In the present study, intra-observer reproducibility in classifying polyps to non-neoplastic and neoplastic pit patterns was high; however, inter-observer reproducibility was unsatisfactory.

In the present study, simplifications in interpretation of the pit pattern, grouping pit patterns in non-neoplastic and neoplastic categories were made. Huang *et al.* [9] suggested that such approach could lead to diminishing the potential of Kudo's classification. This approach is in the authors' opinion acceptable in the study with a limited number of cases. Another limitation in our study is potential biases resulting from interpretation of recordings, which can be somewhat different from the real time evaluation of colorectal lesions [9]. We tried to overcome such limitations by interpreting each polyp not only using still pictures but also videofilms. It should also be remembered that different pit patterns may be present within one polyp (e.g. in serrated adenoma) [9].

In conclusion, acetic-acid magnification endoscopy is of a limited value in predicting neoplastic histopathology of small colorectal polyps. Intra-observer reproducibility in classifying small colorectal polyps to particular pit patterns is acceptable, although its inter-observer reproducibility is unsatisfactory.

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