sciendo

PROCEEDINGS OF THE LATVIAN ACADEMY OF SCIENCES. Section B,
Vol. 76 (2022), No. 5/6 (740/741), pp. 650–656.

DOI: 10.2478/prolas-2022-0100

Original Paper

COMPARISON OF NICE CLASSIFICATION FOR OPTICAL DIAGNOSIS OF COLORECTAL POLYPS AND MORPHOLOGY OF REMOVED LESIONS DEPENDING ON LOCALISATION IN COLON

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The narrow-band imaging (NBI) International Colorectal Endoscopic (NICE) classification is based on narrow-band pictures of colon polyps viewed through a narrow-band spectrum. The categorisation utilises staining, surface structure, and vascular patterns to differentiate between hyperplastic and adenomatous colon polyps. It is known that accuracy of the NICE classification for colorectal polyps varies depending on the localisation in the colon.The aim of this study was to compare the diagnostic accuracy of the NICE classification and the gold standard — morphological analysis for the determination of the type of colorectal lesions depending on localisation in colon. A prospective study was performed in an outpatient clinic. 1214 colonoscopies were performed by two expert endoscopists and 475 polyps were found in 291 patients. The overall diagnostic accuracy of the NICE classification was 80.3%. Optical verification was better in ascending colon — 93.9%, followed by sigmoid colon — 82.1%. Inferior results were found for the descending colon — 64.0%. The results of this study showed that the NICE classification could be a helpful instrument in daily practice for the ascending and sigmoid colon. For better results, proper training should be considered. The NICE system could have a role in the replacement of morphological analysis if appropriate results of verification could be achieved.

Keywords: *colonoscopy, colon adenomas, colorectal cancer, endoscopy.*

INTRODUCTION

Colorectal cancer (CRC) is still a serious health issue around the world, with a high fatality rate. CRC is the most frequent type of cancer disease of the digestive tract both globally and in Latvia. In 2018, there were 1.8 million cases of CRC worldwide, with 881 000 deaths (Bray *et al*., 2018). In 2020, in Latvia, 1720 were diagnosed with colorectal cancer, and 671 patients died because of the disease (Global Cancer Observatory, 2020).

In the USA, an estimated 104 270 new cases of CRC were identified in 2021, and 52 980 deaths (American Cancer Society, 2021). It is the third and fourth most prevalent cancer diagnosed in the USA and the United Kingdom, respectively, and the second greatest cause of cancer-related fatalities in both nations (Arnold *et al*., 2017).

The incidence of CRC appears to climb in tandem with a country's human development index and as less developed countries embrace a more Western lifestyle (Schreuders *et al*., 2015).

By 2030, CRC is anticipated to rise by 60% to more than 2.2 million new cases and 1.1 million cancer deaths (Arnold *et al*., 2017).

Generally, CRC continues to be a significant health and socioeconomic problem in developed countries. In contrast to many European countries that have created an organised approach, CRC screening in the United States and also in Latvia is mostly opportunistic. The systems typically offer ad hoc or fee-based services, whereas population-based organised approaches necessitate the measurement and reporting of screening quality at every stage of the process (Song *et al*., 2020).

The majority of CRC are caused by two types of precancerous polyps: adenomatous polyps or sessile serrated lesions (SSL) (Nagtegaal *et al*., 2020). Precancerous polyps usually have distinct characteristics that can be seen during a colonoscopy. Adenomatous polyps typically are well delineated with an elevated appearance and may have a stalk or pedicel, whereas SSL are flat (non-pedunculated) and have a "mucus cap" with indistinct polyp margins (Kolb *et al*., 2017).

Colonoscopy is the gold standard for finding and removing colorectal polyps. It is used to examine the colon mucosa and detect CRC and colorectal polyps. It has been proven to be the most efficient approach for finding colon neoplasms in people over 50 years old and younger patients at high risk of cancer. CRC can be prevented by a colonoscopy and polypectomy, which lowers the disease's fatality rate (Cappell, 2008).

Adenocarcinomas make up about 95% of all CRC. Polyps that are very little (less than 5 mm) and small (6–10 mm) are the most dominant. It is recognised that these polyps (tubular adenomas and sedimentary serum polyps) have a low malignant potential at first and that hyperplastic polyps (HP) have no inclination to malignant transformations (Hassan *et al*., 2010).

The narrow-band imaging (NBI) International Colorectal Endoscopic (NICE) classification is a diagnostic tool for determining colorectal polyp histology based on NBI without optical magnification. NICE is based on narrow-band images of colon polyps through a narrow-band spectrum. The classification uses staining, surface structure, and vascular patterns to differentiate between HP and adenomatous colon polyps. The classification is mainly used for small polyps (< 5 mm or < 10 mm), and colorectal lesions are divided into three categories: type 1 lesions can be removed or observed; type 2 lesions must be polypectomied, and type 3 lesions must be removed endoscopically, if possible (endoscopic submucosal dissection or endoscopic mucosectomy), or surgically (Hewett *et al*., 2012).

It is known that the accuracy of the NICE classification depends on polyp size and visual appearance in the colon (pedunculated versus non-pedunculated polyps). It is suspected that the accuracy of the NICE classification system could vary in different parts of the colon.

The aim of this study was to compare diagnostic accuracy of the NICE classification and the gold standard — morphological analysis for the determination of the type of colorectal lesion depending on localisation in colon.

MATERIALS AND METHODS

Study design. During the period of the study, 1214 patients underwent colonoscopy. The indication of the mentioned procedure was suspected colorectal polyps. The following inclusion criteria were applied: ≥ 18 years old patients, no previous history of colonic surgery, and no previous history of CRC. The population of this study consisted of patients of both sexes who underwent a colonoscopy due to suspected colorectal polyps. The indications for colonoscopy for patients younger than 40 years were cancerophobia, family history of colorectal cancer, changed bowel movement, visible blood in the stool, and a positive faecal occult blood test.

A prospective single center study was performed at the Unit of Gastroenterology and Endoscopy of the Center of Diagnostics in Rīga, Latvia from September 2020 until September 2021. The study was performed in an outpatient clinic by two expert gastrointestinal endoscopists (each of them had performed more than 5000 colonoscopies using narrow-band imaging for better optical verification of colorectal lesions). an Olympus EVIS EXERA III (CF-HQ190L/l) video colonoscope without image magnification was used in polyp analysis. Only full colonoscopies (when intubation of cecum was performed) were included in this study. The withdrawal time of colonoscope from cecum was determined not less than 7 minutes and mucosa of the colon was inspected by white light. All polyps found in the colon were inspected additionally by narrow-band imaging and classified by NICE classification. All polyps were removed by cold, hot snaring or using the mucosectomy technique. If suspected of an invasive lesion, specimens were taken from polyp, and the patient was referred for surgical resection. All removed polyps and specimens from biopsied lesions were transmitted to the Academic Histology laboratory (Rīga, Latvia) for morphological diagnostics. All samples were analysed by expert pathologists.

All lesions were characterised using a narrow-band spectrum by the international NICE classification without image

magnification, and also by size — diminutive (1–5 mm), small (6–9 mm), and large (≥ 10 mm). The size of each polyp was specified using open biopsy forceps or polypectomy snare. Information about the patient and each colorectal lesion (localisation and size) was collected in a specially designed database.

All removed and biopsied lesions were analysed and characterised according to the World Health Organisation criteria depending on morphological characteristics. All lesions were described as serrated polyps and lesions, low-grade dysplasia (LGD), high-grade dysplasia (HGD), superficial submucosal invasive carcinoma (SM-s; < 1000 μm of submucosal invasion) and deep submucosal invasive carcinoma (SM-d; ≥ 1000 μm of submucosal invasion). No traditional serrated adenoma (TAS), sessile serrated lesion with dysplasia (SSL-D) or unclassified serrated adenoma were found morphologically. This information also was collected in a specially designed database.

The type of lesion according to the NICE classification was compared to the morphological result.

Statistical analysis. The diagnostic performance — negative predictive value (NPV), positive predictive value (PPV), specificity, sensitivity, and accuracy were assessed for each type in the NICE classification depending on the localisation in the colon. To identify the uncertainty of the estimates, 95% CI were calculated. McNemar's test was utilised to compare specificity and sensitivity at the patient level. All statistical analyses were two-sided, and *p*-values < 0.05 were deemed statistically significant. SPSS version 24 (IBM Corp., Armonk, NY, USA) was employed for all statistical analyses.

Ethical considerations. The study was carried out in compliance with the ethical principles of the 1975 Helsinki Declaration of the World Health Organisation and their 1983 amendments (World Medical Association, 2013). The study protocol was approved by the Ethics Committee of Rīga Stradiņš University (Nr. 6-1/08/ 3). Each patient provided informed consent.

RESULTS

Study participants and polyp description. The total of 291 patients were included in the study: 139 (47.8%) males and 152 (52.2%) females; age 21 to 82. Figure 1 shows the age distribution of participants included in the study (the median age was 54.9; interquartile range (IQR): 44.7–64.0). There was no significant correlation between size of the polyp and patient age and sex ($p > 0.05$). Detailed data of patient characteristics and the number of polyps that were diagnosed are summarieed in Table 1.

In our study group, most patients — 188 (64.5%) had only one polyp in the colon. Figure 2 shows a detailed distribution of number of patients and number of polyps that were found in the colon.

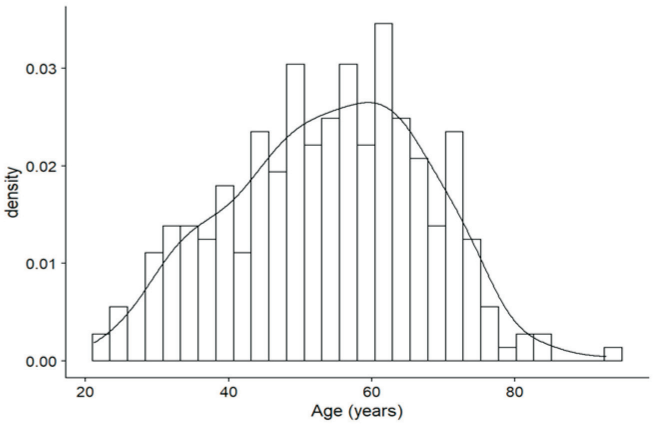

Fig. 1. Age distribution of patients included in the study.

Table 1. Description of patients included in the study

	n	%
Sex of the patient		
Male	139	47.8
Female	152	52.2
Age (years) group		
< 40	51	17.7
40–44	18	6.5
45–50	41	14.0
51–60	77	26.3
61–70	72	24.6
71–75	26	8.9
> 76	6	2.0
Median age (years) by sex		
male	56.7 (43.9–61.8)	
female	53.3 (45.5–65.5)	
Number of analysed polyps per patient		
1	188	64.5
2	70	24.1
3	13	4.5
> 4	20	6.9

n, number

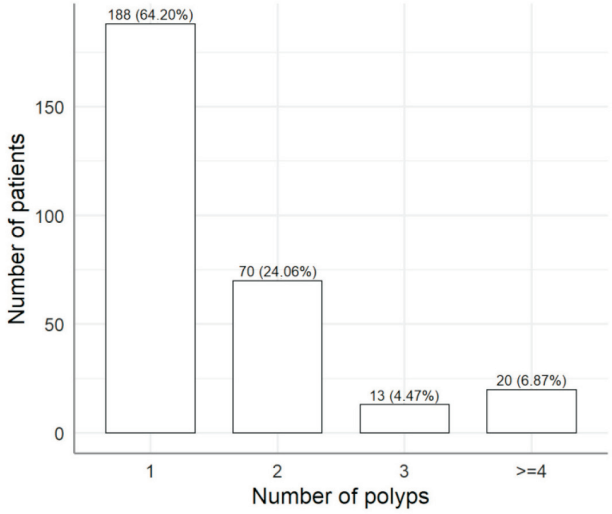

Fig. 2. Distribution of number of patients over number of polyps.

All polyps were categorised by size into three groups: diminutive (1–5 mm), small (6–9 mm), and large (≥ 10). The grouping of polyps by size is shown in Figure 3. The majority (409, 86.1%) of all polyps were flat and only 66 (13.9%) were pedunculated.

In total, polyps were more commonly found in the rectum (223, 46.9%), and less in the ascending colon — 82 (17.3%), and in the sigmoid colon — 78 (16.4%). Figure 4 shows the number of polyps in each segment of the colon.

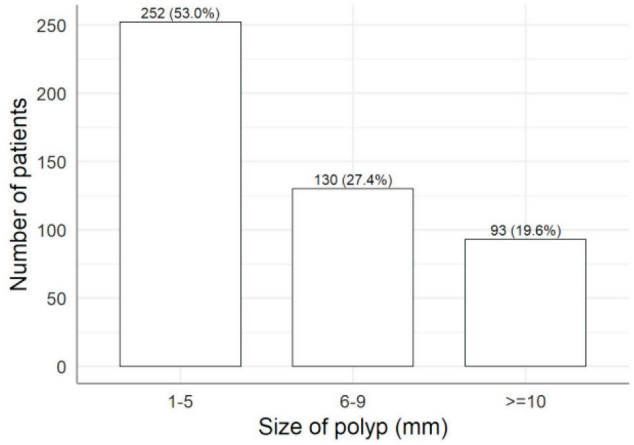

Fig. 3. Distribution of polyps by size.

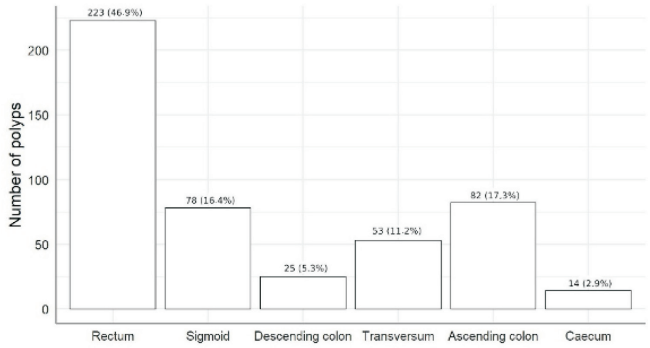

Fig. 4. Number of polyps in each segment of the colon.

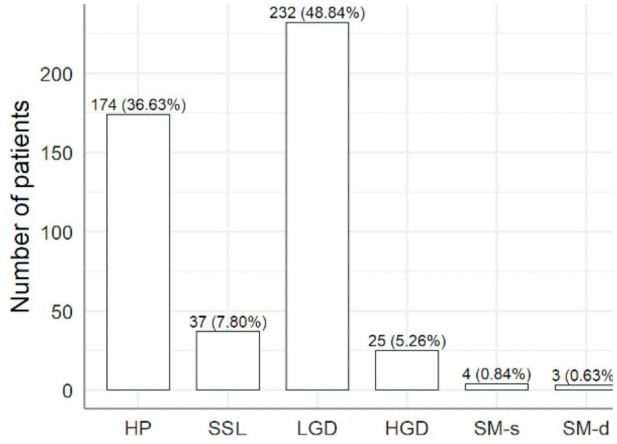

Fig. 5. Distribution of polyps by histological diagnosis.

HP, hyperplastic polyps; SSL, sessile serrated lesions; LGD, low-grade dysplasia; HGD, high-grade dysplasia; SM-s, superficial submucosal invasive carcinoma; SM-d, deep submucosal invasive carcinoma

All polyps were categorised by morphological features. 174 (36.6%) of all polyps were found as a HP, 37 (7.8%) as a SSL, 232 (48.8%) — LGD, 25 (5.3%) — HGD, four (0.8%) were superficial submucosal invasive carcinomas (SM-s), and three (0.6%) were deep submucosal invasive carcinomas (SM-d). Figure 5 shows the distribution of polyps by histological diagnosis.

The characteristics of polyps are summarised in Table 2.

Diagnostic accuracy of the NICE classification. 271 (57.0%) of all polyps were optically diagnosed as NICE type 1 polyps, 198 (41.7%) polyps as NICE type 2 polyps, and only 6 (1.3%) polyps were predicted as NICE type 3 polyps (Fig. 6).

The number of polyps in each colon part, classification by NICE type and morphological features according to NICE classification are shown in Table 3.

Table 2. Description of polyps included in the study

	n	%
Sex of the patient		
Male	227	47.8
Female	248	52.2
Age (years) group		
< 40	68	14.3
40-44	37	7.8
45-50	63	13.3
51-60	129	27.2
61-70	103	21.7
71-75	62	13.1
> 76	13	2.7
Polyp location		
rectum	223	46.9
sigmoid colon	78	16.4
descending colon	25	5.3
transverse colon	53	11.2
ascending colon	82	17.3
caecum	14	2.9
Polyp size (mm)		
Diminutive, 1–5 mm	252	53.0
Small, 6–9 mm	130	27.4
Large, 10 mm	93	19.6
NICE classification		
NICE type 1	271	57.0
NICE type 2	198	41.7
NICE type 3	6	1.3
Histological diagnosis		
HP	174	36.6
SSL	37	7.8
LGD	232	48.8
HGD	25	5.3
SM-s	4	0.8
SM-d	3	0.6

n, number; HP, hyperplastic polyps; SSL, sessile serrated lesions; LGD, low-grade dysplasia; HGD, high-grade dysplasia; SM-s, superficial submucosal invasive carcinoma; SM-d, deep submucosal invasive carcinoma

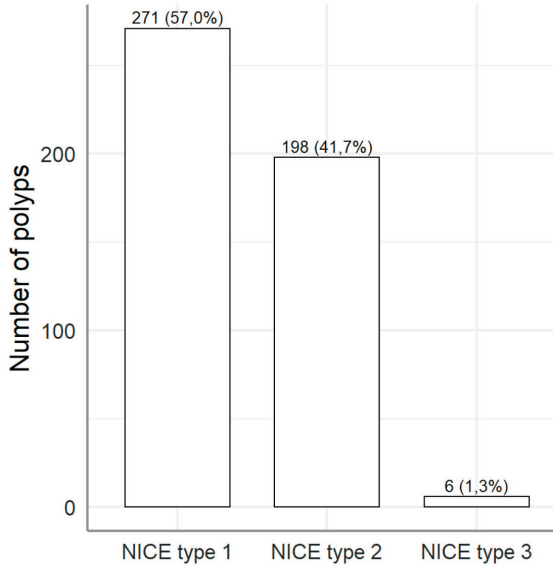

Fig. 6. Distribution of polyps by NICE classification.

The total diagnostic accuracy of the NICE classification in this study was 80.29%. The diagnostic performance for each NICE classification type when stratified by polyp morphological analysis is presented in Table 4.

DISCUSSION

The main method to prevent colorectal cancer still is a colonoscopy with polypectomy. The morphological analysis

Table 3. Morphological features of polyps according to NICE classification

		Histopathological diagnosis					
Type of NICE classification	n	HP	SSL	LGN	HGN	SM-s	SM-d
NICE Type 1							
rectum	149	94	4	49	2	0	0
sigmoid	30	19	2	8	1	0	0
colon descending	16	8	0	6	2	0	0
colon transverse	24	10	6	7	1	0	0
colon ascending	44	28	16	0	0	0	0
caecum	8	3	3	1	1	0	0
NICE Type 2							
rectum	71	1	1	65	3	0	1
sigmoid	47	4	1	38	4	0	0
colon descending	8	1	0	5	2	0	0
colon transverse	29	3	1	21	4	0	0
colon ascending	37	3	2	28	4	0	1
caecum	6	0	1	4	1	0	0
NICE Type 3							
rectum	3	0	0	0	0	2	1
sigmoid	1	0	0	0	0	1	0
colon descending	1	0	0	0	0	1	0
colon transverse	0	0	0	0	0	0	0
colon ascending	1	0	0	0	0	0	0
caecum	0	0	0	0	0	0	0

n, number of polyps; HP, hyperplastic polyps; SSL, sessile serrated lesions; LGD, low-grade dyspasia; HGD, high-grade dysplasia; SM-s, superficial submucosal invasive carcinoma; SM-d, deep submucosal invasive carcinoma

Table 4. Diagnostic accuracy of each type of NICE classification stratified by polyp histopathological diagnosis

Type of NICE classification	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	Accuracy (%) (95% CI)
NICE Type 1					
rectum	98.04 (93.10–99.76)	60.16 (50.95–68.88)	67.11 (58.95–74.58)	97.37 (90.82–99.68)	77.33 (71.30–82.63)
sigmoid	80.77 (60.65–93.45)	82.69 (82.69–91.77)	70.00 (50.60–85.27)	89,58 (77.34–96.53)	82,05 (71.72–89.83)
colon descending	88.89 (51.75–99.72)	50.00 (24.65–75,35)	50.00 (24.65–75.35)	88.89 (51.75–99.72)	64.00 (42.52–82.03)
colon transverse	80.00 (56.34–94.27)	75.76 (57.74–88.91)	66.67 (44.68–84.37)	86.21 (68.34–96.11)	77.36 (63.79–87.72)
colon ascending	89.80 (77.77–96,.60)	100.00 (89.42–100)	100.00 (91.96–100)	86.84 (71.91–95.59)	93,.90 (86.34–97.99)
caecum	85.71 (42.13–99.64)	71.43 (29.04–96.33)	75.00 (34.91–96,.81)	83.33 (35.88–99.58)	78.57 (49.20–95.34)
NICE Type 2					
rectum	58.47 (49.04–67.47)	98.13 (93.41–99.77)	97.18 (90.19–99.66)	68.18 (60.20–75.45)	77.33 (71.30–82.63)
sigmoid	82.35 (69.13–91.60)	81.48 (61.92–93.70)	89,.36 (76.90–96.45)	70.97 (51.96–85.78)	82.05 (71.72–89.83)
colon descending	46.67 (21.27–72.41)	90.00 (55.50–99.75)	87.50 (47.35–99.68)	52.94 (27.81–77.02)	64.00 (42.52–82.03)
colon transverse	75.76 (57.74–88.91)	80.00 (56.34–94.27)	86.21 (68.34–96.11)	66.67 (44.68–84.37)	77.36 (63.79–87.72)
colon ascending	100.00 (89.42–100)	89.80 (77.77–96.60)	86.84 (71.91 –95.59)	100 (91.96–100.00)	93.90 (86.34–97.99)
caecum	71.43 (29.04–96.33)	85.71 (42.13–99.64)	83.33 (35.88 –99.58)	75.00 (34.91–96.81)	78.57 (49.20–95.34)
NICE Type 3					
rectum	100 (47.82–100)	100 (98.34–100)	100 (47.82–100)	100 (98.34–100)	100 (98.37–100)
sigmoid	100 (2.50–100)	100 (95.32–100)	100 (2.50–100)	100 (95.32–100)	100 (95.38–100)
colon descending	100 (2.50–100)	100 (85.75–100)	100 (2.50–100)	100 (85.75–100)	100 (86.28–100)
colon transverse	-	-	-	-	-
colon ascending	-	-	-	-	-
caecum	-	-	-	-	-

95% CI, 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value

of removed polyps is an expensive method, so alternative solutions are being searched for. One of the tools to predict the morphological signs of a polyp found in the colon could be the NICE classification. Studies with large numbers of polyps should be performed in order to start using the NICE classification system in clinical practice.

The current study reports the results of comparing diagnostic accuracy of the NICE classification and morphological analysis for the determination of the type of colorectal lesions depending on localisation in the colon. Our results showed that the overall accuracy of the NICE classification was 80.29%, which is higher compared to that estimated in a similar study (76.7%) (Patrun *et al*., 2018). It is known that the accuracy of the NICE classification depends on the type of polyp (Patrun *et al*., 2018).

The accuracy of NICE classification system in ascending colon overall reached 93.90% with sensitivity 89.80% and 100% for NICE type 1 and NICE type 2 polyps, respectively. Those results could be explained by fact that SSL are mostly found in the right colon and endoscopists suspect Type 1 polyps in this localisation more often. Despite the fact that most of the polyps found in the right colon are Type 1 lesions, their morphological features must be taken into account. The NICE classification is not intended to differentiate between HP and SSL. A previous study (Sano *et al*., 2020) emphasised the intricacy of differentiation between both type 1 lesions. SSL usually appears by a red cap sign, a cloud-like surface with dilated and branched vessels, and expanded crypt openings (Sano *et al*., 2020); those signs should be taken into account when differentiating between HP and SSL. The purpose of this study was not to differentiate between both type 1 polyps, and therefore, there is no data about the accuracy of NICE classification for each Type 1 lesion.

In the sigmoid colon, accuracy for type 1 and type 2 polyps was 82.05%, with sensitivity 80.77% and 82.35%, respectively; for the type 3 polyp, accuracy and sensitivity were 100%. In the sigmoid colon the most suspected polyps usually are adenomas. In this study, in sigmoid colon, 42 of 78 polyps were adenomatous and the endoscopist predicted that 47 of 78 could be adenomas. These results could be explained by the fact that in the distal part of the sigmoid colon, HP is found more often. The fact that different morphological features of type 2 lesions are possible should be taken into account. Optical diagnosis using NICE classification is an important tool for differentiation between LGD and HGD lesions and between superficial and deep submucosal invasive carcinoma. The correct classification helps to make a decision about the correct therapeutic strategy (endoscopically or surgical resection) and intervals of control colonoscopy to avoid interval cancers.

In the cecum, accuracy of the NICE classification system for type 1 and type 2 polyps was 78.57% with sensitivity 85.71% and 71.54% and specificity 71.43% and 85.71%, respectively. In the cecum 14 polyps were found. Eight of them were classified as type 1 polyps and histopathological analysis revealed that two of them were adenomas. Six of all cecum polyps were classified as type 2 lesions and one of them was SSL. Analysis of the data on cecal polyps whoed that there still are difficulties in morphological verification of SSL. Usually, when there is a discussion about precancerous lesions of the colon, adenomatous polyps are mostly mentioned. However, SSL must not be forgotten in the carcinogenic process of colorectal cancer. It is known that approximately 20% of all CRC cases develop through a serrated pathway (Kahi *et al*., 2012). SSL are challenging lesions during colonoscopy, and the visualisation of these polyps is complicated because of the flat shape, mucus cup on the surface of polyps and cloudy borders (Pohl *et al*., 2013). The optical differentiation of that kind of lesion is not simple and the wrong decision of polyp type could be made during endoscopy. Similar to HP, SSL has specific crypts, which is the reason why these two types of polyps are still misclassified.

Tables 3 and 4 show which part of the colon and which polyp type are misclassified more often. It is seen that NICE 1 and NICE 2 types are misclassified most often, especially in the descending colon. This suggests that misclassification can result in increased procedural costs, and further constant education of endoscopists should be planned in the future. Training should include the recognition of vascular and mucosal patterns of colonic polyps.

Still, the current topic of detecting and recognising the type of polyp is the quality of colonoscopies. It must be controlled at the national level. All quality criteria like cecal intubation, instrument evacuation time, double right side inspection, adenoma detection rate, and preprocedural colon cleanliness must be taken into account. Also, there are some other additional methods that could improve the accuracy of the NICE classification. For example, use of a cap on the top of colonoscope for stabilisation of the image of the polyp, thorough rinsing of a visible lesion using simethicone or other foam removers to clean the mucosae from faecal leftovers.

The "Near focus" function could also be helpful to determine the type of the polyp and to make a decision on the management of the lesion found in the colon. Use of magnifying endoscopes could be helpful, especially for diminutive lesions.

Despite the fact that our study reported significant results, there are several limitations to this study. Firstly, only one study centre was included in the study. Secondly, only two expert endoscopists performed colonoscopies with polyp detection and classification using the NICE system.

Further multicentre studies with a larger number of endoscopists must be performed and serious, long-lasting, permanent training of colorectal lesions classification by the NICE system must be implemented to start using the NICE classification system in full.

CONCLUSIONS

The results of this study show that the NICE classification could be a helpful instrument in daily practice for the ascending and sigmoid colon. In those localisations, the best accuracy rates were reached for NICE type 1 and type 2 polyps. The worst accuracy results were reached in the descending colon for NICE type 1 and type 2 polyps, which indicates that more attention must be payed to the segment between the sigmoid and transverse colon.

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Received 19 March 2022
Accepted in the final form 10 May 2022

NICE KLASIFIKĀCIJAS OPTISKAI KOLOREKTĀLO POLIPU DIAGNOSTIKAI UN NOŅEMTO VEIDOJUMU MORFOLOĢIJAS SALĪDZINĀJUMS ATKARĪBĀ NO LOKALIZĀCIJAS RESNAJĀ ZARNĀ

NICE klasifikācija (NBI Starptautiskā kolorektālā endoskopiskā klasifikācija) balstās uz zarnu polipu attēliem, kas iegūti, tos aplūkojot šaurās gaismas joslas spektrā. Klasifikācijā tiek aplūkots krāsojums, virsmas struktūra, asinsvadu zīmējums, kas ļauj diferencēt hiperplastiskus un adenomatozus resnās zarnas polipus. Ir zināms, ka kolorektālo polipu NICE klasifikācijas precizitāte atšķiras atkarībā no to lokalizācijas resnajā zarnā. Šī pētījuma mērķis bija salīdzināt NICE klasifikācijas un zelta standarta — morfoloģiskās analīzes — diagnostisko precizitāti kolorektālo polipu noteikšanai atkarībā no to lokalizācijas resnajā zarnā. Tika veikts prospektīvs pētījums ambulatorā klīnikā. Divi pieredzējuši endoskopisti veica kopumā 1214 kolonoskopijas, un 291 pacientam tika konstatēti kopumā 475 polipi. NICE klasifikācijas kopējā diagnostiskā precizitāte bija 80,3%. Optiskā kolorektālo polipu diagnostika visprecīzākā bija augšupejošajā zarnā — 93,9%, kam seko sigmveida zarna — 82,1%. Zemāki rezultāti tika novēroti lejupejošās zarnas polipu diagnostikā — 64,0%. Pētījumā iegūtie rezultāti norāda, ka NICE klasifikācija varētu būt noderīga ikdienas praksē augšupejošās un sigmveida zarnas polipu diagnostikā. Labāku rezultātu iegūšanai būtu nepieciešama atbilstoša endoskopistu apmācība. Ja tiktu sasniegti atbilstoši verifikācijas rezultāti, NICE klasifikācijai varētu būt nozīme morfoloģiskās analīzes aizstāšanā.