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Retrospective Study

Diagnostic performance of endoscopic classifications for neoplastic lesions in patients with ulcerative colitis: A retrospective case-control study

Yuichi Kida, Takeshi Yamamura, Keiko Maeda, Tsunaki Sawada, Eri Ishikawa, Yasuyuki Mizutani, Naomi Kakushima, Kazuhiro Furukawa, Takuya Ishikawa, Eizaburo Ohno, Hiroki Kawashima, Masanao Nakamura, Masatoshi Ishigami, Mitsuhiro Fujishiro

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Abstract

BACKGROUND

It is unclear whether the Japan Narrow-Band Imaging Expert Team (JNET) classification and pit pattern classification are applicable for diagnosing neoplastic lesions in patients with ulcerative colitis (UC).

AIM

To clarify the diagnostic performance of these classifications for neoplastic lesions in patients with UC.

METHODS

This study was conducted as a single-center, retrospective case-control study. Twenty-one lesions in 19 patients with UC-associated neoplasms (UCAN) and 23 lesions in 22 UC patients with sporadic neoplasms (SN), evaluated by magnifying image-enhanced endoscopy, were retrospectively and separately assessed by six endoscopists (three experts, three non-experts), using the JNET and pit pattern classifications. The results were compared with the pathological diagnoses to evaluate the diagnostic performance. Inter- and intra-observer agreements were

calculated.

RESULTS

In this study, JNET type 2A and pit pattern type III/IV were used as indicators of low-grade dysplasia, JNET type 2B and pit pattern type V₁ low irregularity were used as indicators of high-grade dysplasia to shallow submucosal invasive carcinoma, JNET type 3 and pit pattern type V₁ high irregularity/V_N were used as indicators of deep submucosal invasive carcinoma. In the UCAN group, JNET type 2A and pit pattern type III/IV had a low positive predictive value (PPV; 50.0% and 40.0%, respectively); however, they had a high negative predictive value (NPV; 94.7% and 100%, respectively). Conversely, in the SN group, JNET type 2A and pit pattern type III/IV had a high PPV (100% for both) but a low NPV (63.6% and 77.8%, respectively). In both groups, JNET type 3 and pit pattern type V₁-high irregularity/V_N showed high specificity. The inter-observer agreement of JNET classification and pit pattern classification for UCAN among experts were 0.401 and 0.364, in the same manner for SN, 0.666 and 0.597, respectively. The intra-observer agreements of JNET classification and pit pattern classification for UCAN among experts were 0.387, 0.454, for SN, 0.803 and 0.567, respectively.

CONCLUSION

The accuracy of endoscopic diagnosis using both classifications was lower for UCAN than for SN. Endoscopic diagnosis of UCAN tended to be underestimated compared with the pathological results.

Key Words: Diagnostic performance; Japan Narrow-Band Imaging Expert Team classification; Pit pattern classification; Sporadic neoplasms; Ulcerative colitis; Ulcerative colitis-associated neoplasms

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Core Tip: This retrospective case-control study evaluated the diagnostic performance of the Japan Narrow-Band Imaging Expert Team (JNET) and pit pattern classifications for neoplastic lesions in patients with ulcerative colitis (UC). The JNET and pit pattern classifications did not show high accuracy in diagnosing the pathology and invasion depth of neoplastic lesions in patients with UC. Endoscopic diagnosis of UC-associated neoplasms tended to be underestimated when compared with pathological results. Endoscopic diagnosis of neoplastic lesions in patients with UC is still difficult, and treatment strategies need to be carefully determined.

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INTRODUCTION

Patients with long-standing ulcerative colitis (UC) are at risk for colorectal tumors due to chronic inflammation. The cumulative risk of colorectal cancer at 10, 20, and 30 years after UC onset are reportedly 1.6%, 8.3%, and 18.4%, respectively[1]. Consequent to improvements in UC treatment, long-standing UC cases have gradually increased, and surveillance colonoscopy has become more important. UC patients are exposed to the risk of not only UC-associated neoplasms (UCAN) but also sporadic neoplasms (SN). As the treatment strategy for UCAN greatly differs from that for SN, distinguishing UCAN from SN is important[2]. In line with the Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations (SCENIC) consensus statement, endoscopic resection now tends to be accepted as a treatment for endoscopically visible dysplasia[3]. With the support from the SCENIC consensus statement, endoscopic treatments for visible dysplasia have gradually increased and have attracted attention recently[4-6].

UCAN differentiation by endoscopic findings had been described previously. Prior studies revealed that features of surface structure and vascular pattern obtained by magnifying Narrow-Band Imaging (NBI) and chromoendoscopy are useful in diagnosing UCAN[7-11]. Additionally, multimodal endo-

Table 1 Clinical characteristics of ulcerative colitis patients with neoplastic lesions (mean ± SD)

	UCAN group (n = 19)	SN group (n = 22)	P value
Age at UC onset (yr)	35.7 ± 10.9	48.8 ± 14.6	0.003 ^a
Disease duration (yr)	17.8 ± 9.4	12.9 ± 10.7	0.120 ^a
Sex			0.829 ^b
Male	11	12	
Female	8	10	
Extent of disease			0.231 ^b
Total colitis	16	14	
Left-sided colitis	3	6	
Proctitis	0	2	
Clinical type			0.139 ^b
Relapse and remission	10	15	
Chronic persistent	9	5	
First attack	0	2	
Pathological type			< 0.001 ^b
LGD	2	16	
HGD	11	5	
Shallow submucosal invasive carcinoma	3	0	
Deep submucosal invasive carcinoma	5	2	
Primary sclerosing cholangitis	1	0	0.463 ^c
Family history of colorectal cancer	1	2	0.639 ^c

^aStudent *t*-test.^bChi-square test.^cFisher's exact test.

P < 0.05 was considered statistically significant. SD: Standard deviation; HGD: High-grade dysplasia; LGD: Low-grade dysplasia; SN: Sporadic neoplasms; UC: Ulcerative colitis; UCAN: Ulcerative colitis-associated neoplasms.

scopic classification without the use of magnifying endoscopy has been reported[12]. Most of these studies focused on differentiating neoplastic from non-neoplastic lesions or on detecting these lesions, not on qualitatively diagnosing neoplastic lesions in UC patients. While several studies have focused on differentiating UCAN from non-neoplastic lesions, few reports have explored the differentiation of UCAN from SN[2].

The Japan NBI Expert Team (JNET) and pit pattern classifications are useful for determining the pathology and invasion depth of colorectal tumors[13,14]. Both classifications have high reproducibility and good diagnostic accuracy in terms of pathology and invasion depth[15-19], as well as good intra- and inter-observer agreement rates for diagnosing colorectal tumors[18,20]. Dysplastic pit patterns are sometimes observed even in non-dysplastic lesions due to inflammation and regenerative changes in UC patients[21]. Surface and vascular patterns are modified by inflammation in UCAN[22]. These patterns are likely to be modified by inflammation not only in UCAN but also in SN located in the inflamed mucosa. Therefore, whether these endoscopic classifications apply to the diagnosis of neoplastic lesions in UC patients remains unclear. Only a few reports have described the usefulness of both classifications in diagnosing UCAN[22], and there have been no reports on their use for classifying SN in UC patients. Hence, the present retrospective case-control study aimed to evaluate the diagnostic performance of the JNET and pit pattern classifications for neoplastic lesions in UC patients.

MATERIALS AND METHODS

Patients

A total of 89 UC patients who had neoplastic lesions that could be pathologically evaluated by biopsy, endoscopic resection, or surgery and who underwent colonoscopy at Nagoya University Hospital from

Table 2 Characteristics of endoscopic and macroscopic findings

	UCAN group (n = 21)	SN group (n = 23)	P value
Tumor location			0.044 ^a
Proctosigmoid colon	17	12	
Others	4	11	
Tumor color			0.032 ^a
Red	15	9	
Pale or the same as the surrounding mucosa	6	14	
Lesion border			< 0.001 ^a
Clear	5	23	
Unclear	16	0	
Tumor morphology			0.173 ^a
Pedunculated	0	0	
Sessile	8	7	
Superficial elevated	7	14	
Flat	2	0	
Depressed	4	2	
UCEIS (median, range)	2 (0–4)	0 (0–5)	< 0.001 ^b

^aChi-square test.^bMann-Whitney *U* test.

P < 0.05 was considered statistically significant. SN: Sporadic neoplasms; UCAN: Ulcerative colitis-associated neoplasms; UCEIS: Ulcerative Colitis Endoscopic Index of Severity.

August 2005 to April 2020 were consecutively registered. Neoplastic lesions located in the colonic mucosa outside the previously or currently inflamed mucosa were excluded. Additionally, lesions magnified using both NBI or Blue LASER imaging (BLI) and chromoendoscopy with indigo carmine or crystal violet were included. The present study ultimately enrolled 41 UC patients with 44 lesions that could be assessed using both the JNET and pit pattern classifications. According to pathological findings, these patients were divided into two groups – namely, the UCAN group, which comprised 19 patients with 21 lesions, and the SN group, which consisted of 22 UC patients with 23 lesions.

Endoscopic evaluation

Endoscopists conducted routine white-light imaging observation. When neoplastic lesions were identified, magnifying NBI or BLI and magnifying chromoendoscopy using indigo carmine or crystal violet were performed. All lesions were endoscopically detectable, visually identified, and subsequently diagnosed using target biopsy. The morphological type of neoplasms was categorized in accordance with the SCENIC consensus statement[3]. The severity of inflammation in the mucosa surrounding neoplasms was assessed using the Ulcerative Colitis Endoscopic Index of Severity (UCEIS)[23]. The JNET and pit pattern classifications were employed to evaluate the pathology and invasion depth of neoplasms by endoscopy. With the JNET classification, lesions were categorized based on surface and vascular patterns into types 1, 2A, 2B, and 3. The pit pattern classification was used under indigo carmine or crystal violet observation; lesions were categorized based on form of crypt orifices into types I, II, III, IV, V₁ low irregularity, V₁ high irregularity, and V_N. This study used JNET type 2A and pit pattern type III/IV as indicators of low-grade dysplasia (LGD), based on previous reports[22]. Furthermore, in the same manner, as LGD, JNET type 2B and pit pattern type V₁ low irregularity were utilized as indicators of high-grade dysplasia (HGD) to shallow submucosal invasive carcinoma (sSM), whereas JNET type 3 and pit pattern type V₁ high irregularity/V_N were used as indicators of deep submucosal invasive carcinoma (dSM). Endoscopic images corresponding to the part that could be evaluated pathologically were extracted, and six endoscopists (three experts, three non-experts) each evaluated the endoscopic findings. Experts were defined as those with ≥ 5-year experience in magnifying image-enhanced endoscopy and who had managed more than 1000 cases[18]. Endoscopists independently evaluated the images obtained from 44 lesions; when individual diagnostic interpretations differed, they discussed the case until a consensus was reached. Diagnostic performance was assessed by consensus of the first diagnosis of three endoscopists. Inter- and intra-observer agreements

were calculated for the diagnostic results of each endoscopist. The second diagnosis was performed by randomly switching the order of images at ≥ 1 mo after the first round of diagnosis to calculate for intra-observer agreement.

Pathological assessment

Two pathologists specializing in the gastrointestinal tract conducted pathological diagnosis of UCAN and SN according to the Riddell *et al*[24]'s pathological system. UCAN and SN were differentiated based on pathological results. If necessary, p53 and Ki-67 immunostaining were performed. UCAN was diagnosed for cases with diffuse and strong expression or complete absence of p53 immunostaining [25]. Differentiation of Ki-67-positive cells from the basal mucosal side toward the superficial mucosal side[25,26], called "bottom-up," was also useful in diagnosing UCAN. Contrary to the UCAN, expression of p53 is low in SN. Moreover, Ki-67-positive cells are mainly distributed at the superficial zone of the mucosal layer, and tumor cells differentiate towards the basal side of the mucosa in the SN [26], also known as "top-down". Dysplasia was classified into LGD and HGD according to the degree of cellular and nuclear dysplastic change. Submucosal invasive carcinoma was divided into dSM and sSM depending on whether the vertical invasion depth exceeded 1000 μm . When two pathologists had different diagnoses, they discussed the case until a conclusion was reached.

Data collection

Clinical data, including age at UC onset, disease duration, sex, disease distribution (total colitis, left-sided colitis, proctitis), clinical type (relapse and remission, chronic persistent, first attack), primary sclerosing cholangitis (PSC), and family history of colorectal cancer, were retrospectively collected from medical records and investigated. Endoscopic findings, including location, color, lesion border, morphology, and UCEIS, were obtained from medical reports and evaluated.

Statistical analysis

Continuous variables were expressed as mean \pm SD or as median with range and were compared using Student's *t*-test or Mann-Whitney *U* test, depending on the normality of data distribution, as determined by the Shapiro-Wilk test. Categorical variables were compared using Fisher's exact test or chi-square test. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated for both the JNET and pit pattern classifications. Inter- and intra-observer agreements were calculated using κ coefficient and arbitrarily interpreted as follows: 0–0.20, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; and 0.81–1.00, excellent. Statistical analysis was conducted using SPSS Statistics version 27 (IBM Corp., Armonk, NY, United States) and R3.6.3 (CRAN, freeware, <https://personal.hs.hirosaki-u.ac.jp/pteiki/research/stat/R/>), with $P < 0.05$ being indicative of statistical significance.

RESULTS

Clinical characteristics

All patients were divided into two groups according to pathological findings. Inter-observer agreement in the diagnosis between UCAN and SN by the two pathologists was 0.531. The clinical characteristics of both groups are summarized in Table 1. The UCAN group had a significantly lower mean age at UC onset than the SN group (35.7 *vs* 48.8 years, $P = 0.003$). Pathological findings indicated 2 LGD lesions, 11 HGD lesions, 3 sSM lesions, and 5 dSM lesions in the UCAN group and 16 LGD lesions, 5 HGD lesions, and 2 dSM lesions in the SN group. No significant differences in the disease duration, sex, extent of disease, disease distribution, presence of PSC, and family history of colorectal cancer were identified between the two groups.

Endoscopic and clinical findings

The endoscopic findings for both groups are presented in Table 2. A total of 17 (81.0%) and 12 (52.2%) lesions were detected in the proctosigmoid colon in the UCAN and SN groups, respectively ($P = 0.044$). The UCAN group had a higher percentage of reddish lesions than the SN group (71.4% *vs* 39.1%, $P = 0.032$). All lesions in the SN group exhibited a clear border, whereas 16 lesions (76.2%) in the UCAN group showed an unclear border ($P < 0.001$). The UCAN group had a higher proportion of flat or depressed lesions than the SN group (28.6% *vs* 8.7%, $P = 0.094$). Inflammation in the mucosa surrounding neoplasms was more severe in the UCAN group than in the SN group [UCEIS (median): 2 *vs* 0, $P < 0.001$].

Diagnostic performance of the JNET and pit pattern classifications

Diagnostic performance for each type in the JNET and pit pattern classifications is shown in Tables 3 and 4, respectively. Sensitivity, specificity, PPV, NPV, and accuracy were calculated for experts and non-experts separately.

Table 3 Diagnostic performance (95% confidence interval) for each type in the Japan Narrow-Band Imaging Expert Team classification

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
UCAN JNET type 2A					
Experts	50.0 (10.2–85.6)	94.7 (90.5–98.5)	50.0 (10.2–85.6)	94.7 (90.5–98.5)	90.5 (82.9–97.3)
Non-experts	100 (36.9–100)	78.9 (72.3–78.9)	33.3 (12.3–33.3)	100 (91.6–100)	81.0 (68.9–81.0)
UCAN JNET type 2B					
Experts	78.6 (64.6–89.5)	57.1 (29.2–79.1)	78.6 (64.6–89.5)	57.1 (29.2–79.1)	71.4 (52.8–86.1)
Non-experts	78.6 (63.8–87.9)	71.4 (41.9–90.0)	84.6 (68.7–94.6)	62.5 (36.6–78.8)	76.2 (56.5–88.6)
UCAN JNET type 3					
Experts	60.0 (27.5–75.9)	93.8 (83.6–98.7)	75.0 (34.4–94.9)	88.2 (78.7–92.9)	85.7 (70.3–93.3)
Non-experts	40.0 (14.9–40.0)	100 (92.2–100)	100 (37.3–100)	84.2 (77.6–84.2)	85.7 (73.8–85.7)
SN JNET type 2A					
Experts	75.0 (62.6–75.0)	100 (71.6–100)	100 (83.4–100)	63.6 (45.5–63.6)	82.6 (65.3–82.6)
Non-experts	87.5 (74.7–92.5)	85.7 (56.4–97.1)	93.3 (79.6–98.7)	75.0 (49.3–85.0)	87.0 (69.1–93.9)
SN JNET type 2B					
Experts	100 (63.4–100)	83.3 (73.2–83.3)	62.5 (39.6–62.5)	100 (87.8–100)	87.0 (71.0–87.0)
Non-experts	80.0 (42.6–96.1)	83.3 (72.9–87.8)	57.1 (30.4–68.7)	93.8 (82.1–98.8)	82.6 (66.4–89.6)
SN JNET type 3					
Experts	50.0 (11.2–50.0)	100 (96.3–100)	100 (22.4–100)	95.5 (91.9–95.5)	95.7 (88.9–95.7)
Non-experts	50.0 (11.2–50.0)	100 (96.3–100)	100 (22.4–100)	95.5 (91.9–95.5)	95.7 (88.9–95.7)

CI: Confidence interval; NPV: Negative predictive value; PPV: Positive predictive value; SN: Sporadic neoplasms; UCAN: Ulcerative colitis-associated neoplasms; JNET: Japan Narrow-Band Imaging Expert Team.

In the UCAN group, JNET type 2A had a low PPV [experts *vs* non-experts: 50.0% (10.2–85.6) *vs* 33.3% (12.3–33.3)] and a high NPV [experts *vs* non-experts: 94.7% (90.5–98.5) *vs* 100% (91.6–100)] for both experts and non-experts. Conversely, in the SN group, JNET type 2A had a high PPV [experts *vs* non-experts: 100% (83.4–100) *vs* 93.3% (79.6–98.7)] and a low NPV [experts *vs* non-experts: 63.6% (45.5–63.6) *vs* 75.0% (49.3–85.0)]. In the UCAN group, the accuracy of diagnosis for JNET types 2A, 2B, and 3 by experts was 90.5%, 71.4%, and 85.7%, respectively, and that by non-experts was 81.0%, 76.2%, and 85.7%, respectively.

In the UCAN group, pit pattern type III/IV had a low PPV [experts *vs* non-experts: 40.0% (14.9–40.0) *vs* 20.0% (7.3–20.0)] and a high NPV [experts *vs* non-experts: 100% (92.2–100) *vs* 100% (88.4–100)] for both experts and non-experts. Conversely, in the SN group, pit pattern type III/IV had a high PPV [experts *vs* non-experts: 100% (86.4–100) *vs* 92.9% (77.8–98.6)] and a low NPV [77.8% (56.6–77.8) *vs* 66.7% (43.3–75.6)]. In the UCAN group, the accuracy of diagnosis for pit pattern type III/IV, type V₁ low irregularity, and type V₁ high irregularity/V_N by experts was 85.7%, 57.1%, and 76.2%, respectively, and that by non-experts was 61.9%, 57.1%, and 85.7%, respectively. The accuracy of diagnosis for JNET type 3 and pit pattern type V₁ high irregularity/V_N by both experts and non-experts was higher in the SN group than in the UCAN group. **Figure 1** shows a representative case of UCAN misdiagnosed by all endoscopists.

Intra-observer and inter-observer agreements for the JNET and pit pattern classifications

Intra-observer agreement was separately calculated for experts and non-experts (**Table 5**). The intra-observer agreement among experts for the JNET classification of UCAN, pit pattern classification of UCAN, JNET classification of SN, and pit pattern classification of SN was 0.387, 0.454, 0.803, and 0.567, respectively. The corresponding values for non-experts were 0.640, 0.569, 0.828, and 0.628, respectively. The intra-observer agreement for SN was higher than that for UCAN. Among non-experts, the intra-observer agreement for both UCAN and SN was higher with the JNET classification than with the pit pattern classification.

Inter-observer agreement was calculated similarly (**Table 6**). The inter-observer agreement among experts for the JNET classification of UCAN, pit pattern classification of UCAN, JNET classification of SN, and pit pattern classification of SN was 0.401, 0.364, 0.666, and 0.597, respectively. The corresponding values for non-experts were 0.237, 0.378, 0.503, and 0.437, respectively. Overall, the inter-

Table 4 Diagnostic performance (95% confidence interval) for each type in the pit pattern classification

	Sensitivity, (%)	Specificity, (%)	PPV, (%)	NPV, (%)	Accuracy, (%)
UCAN pit pattern type III/IV					
Experts	100 (37.3–100)	84.2 (77.6–84.2)	40.0 (14.9–40.0)	100 (92.2–100)	85.7 (73.8–85.7)
Non-experts	100 (36.4–100)	57.9 (51.2–57.9)	20.0 (7.3–20.0)	100 (88.4–100)	61.9 (49.8–61.9)
UCAN pit pattern type VI low irregularity					
Experts	50.0 (35.2–59.8)	71.4 (41.9–91.0)	77.8 (54.8–93.0)	41.7 (24.4–53.1)	57.1 (37.5–70.2)
Non-experts	42.9 (28.4–48.7)	85.7 (56.7–97.3)	85.7 (56.7–97.3)	42.9 (28.4–48.7)	57.1 (37.8–64.9)
UCAN pit pattern type VI high irregularity/VN					
Experts	60.0 (26.1–85.8)	81.3 (70.7–89.3)	50.0 (21.8–71.5)	86.7 (75.4–95.3)	76.2 (60.1–88.5)
Non-experts	60.0 (27.5–75.9)	93.8 (83.6–98.7)	75.0 (34.4–94.9)	88.2 (78.7–92.9)	85.7 (70.3–93.3)
SN pit pattern type III/IV					
Experts	87.5 (75.6–87.5)	100 (72.8–100)	100 (86.4–100)	77.8 (56.6–77.8)	91.3 (74.8–91.3)
Non-experts	81.3 (68.1–86.3)	85.7 (55.6–97.3)	92.9 (77.8–98.6)	66.7 (43.3–75.6)	82.6 (64.3–89.6)
SN pit pattern type VI low irregularity					
Experts	100 (63.4–100)	83.3 (73.2–83.3)	62.5 (39.6–62.5)	100 (87.8–100)	87.0 (71.0–87.0)
Non-experts	60.0 (26.0–85.9)	83.3 (73.9–90.5)	50.0 (21.7–71.6)	88.2 (78.2–95.8)	78.3 (63.5–89.5)
SN pit pattern type VI high irregularity/VN					
Experts	50.0 (11.2–50.0)	100 (96.3–100)	100 (22.4–100)	95.5 (91.9–95.5)	95.7 (88.9–95.7)
Non-experts	50.0 (10.2–85.6)	95.2 (91.4–98.6)	50.0 (10.2–85.6)	95.2 (91.4–98.6)	91.3 (84.4–97.5)

CI: Confidence interval; NPV: Negative predictive value; PPV: Positive predictive value; SN: Sporadic neoplasms; UCAN: Ulcerative colitis-associated neoplasms.

Table 5 Intra-observer agreement

	Experts	Non-experts
UCAN		
JNET classification	0.387 (0.369–0.521)	0.640 (0.566–0.708)
Pit pattern classification	0.454 (0.391–0.509)	0.569 (0.422–0.599)
SN		
JNET classification	0.803 (0.581–0.832)	0.828 (0.686–0.849)
Pit pattern classification	0.567 (0.477–0.595)	0.628 (0.422–0.766)

JNET: Japan Narrow-Band Imaging Expert Team; SN: Sporadic neoplasms; UCAN: Ulcerative colitis-associated neoplasms.

observer agreement for SN was higher than that for UCAN among both experts and non-experts, irrespective of the classification system used.

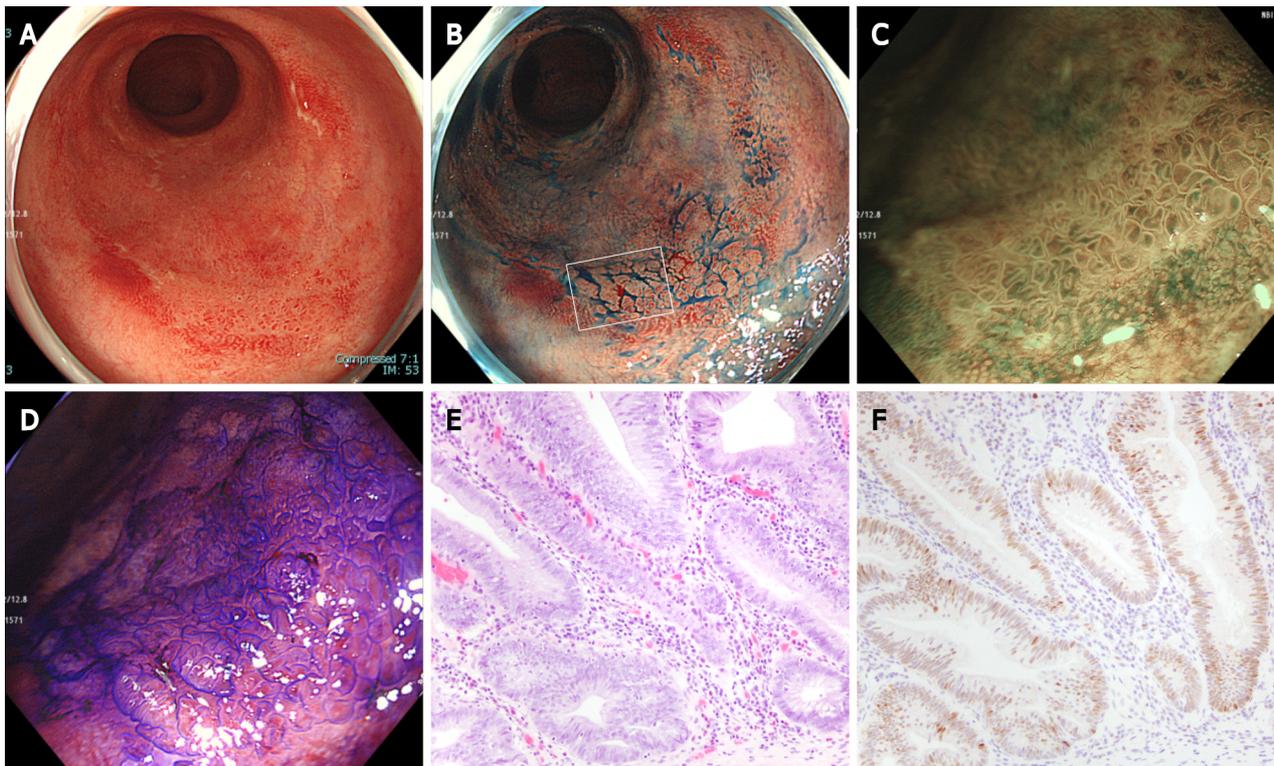
DISCUSSION

In the present study, we evaluated the performance of the JNET and pit pattern classifications in patients with UC. The JNET classification evaluates the tumors' surface and vascular patterns, whereas the pit pattern classification assesses the form of pits on the tumor surface. Colonic mucosal inflammation in UC patients modifies the tumors' surface and vascular patterns and is considered to reduce the diagnostic accuracy of both classifications. Here, we revealed that the accuracy of diagnosing colorectal tumors using JNET and pit pattern classifications was lower in UC patients, particularly those with UCAN, than in non-UC patients[15-18]. The agreement rates were lower for both UCAN and SN

Table 6 Inter-observer agreement

	Experts	Non-experts
UCAN		
JNET classification	0.401	0.237
Pit pattern classification	0.364	0.378
SN		
JNET classification	0.666	0.503
Pit-pattern classification	0.597	0.437

JNET: Japan Narrow-Band Imaging Expert Team; SN: Sporadic neoplasms; UCAN: Ulcerative colitis-associated neoplasms.



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Figure 1 Endoscopic features of ulcerative colitis-associated neoplasms misdiagnosed by all endoscopists. A: White-light imaging reveals a flat elevated lesion in the rectum; B: Chromoendoscopy with indigo carmine shows a clear lesion border; C: Magnifying endoscopy with narrow-band imaging of box in (B) shows regular surface and vascular patterns, which were classified by all endoscopists as Japan Narrow-Band Imaging Expert Team classification type 2A; D: Magnifying endoscopy with crystal violet chromoendoscopy of box in (B) reveals relatively uniform villous structures, which were classified by all endoscopists as pit pattern type IV; E: Pathological examination of the resected specimen by endoscopic submucosal dissection shows architectural atypia. This lesion was pathologically diagnosed as high-grade dysplasia (hematoxylin and eosin staining, original magnification $\times 50$); F: Immunohistochemistry for p53 on serial section of (E).

patients than for non-UC patients. The diagnostic performance of both classifications in UC patients is substantially lower than their previously reported diagnostic performance in non-UC patients[15-18].

Previous reports revealed that, compared to SN, UCAN is more common in the proctosigmoid colon and features more redness, unclear border, flat and depressed lesions, and a higher degree of surrounding inflammation[2]. On magnifying chromoendoscopy, pit pattern types III, IV, and V, which are also caused by regenerative changes, are useful in diagnosing UCAN[9,21]. In the present study, the UCAN group had a significantly higher proportion of lesions with endoscopically unclear border and severe inflammation in the mucosa surrounding neoplasms than the SN group. As colorectal tumors can considerably impact the quality of life of UC patients, it is essential for endoscopists to understand these endoscopic features of UCAN.

Table 7 Diagnostic results of Japan Narrow-Band Imaging Expert Team classification type 2A and pit pattern classification type III/IV in ulcerative colitis-associated neoplasms

	Number	Pathological result		
		LGD (n = 2)	HGD-sSM (n = 14)	dSM (n = 5)
Endoscopist 1				
JNET type 2A	8	1	7	0
Pit type III/IV	7	2	3	2
Endoscopist 2				
JNET type 2A	2	1	1	0
Pit type III/IV	5	2	3	0
Endoscopist 3				
JNET type 2A	2	0	1	1
Pit type III/IV	7	2	5	0
Endoscopist 4				
JNET type 2A	9	2	6	1
Pit type III/IV	8	2	5	1
Endoscopist 5				
JNET type 2A	5	2	2	1
Pit type III/IV	8	2	6	0
Endoscopist 6				
JNET type 2A	7	2	5	0
Pit type III/IV	9	2	6	1

LGD: Low-grade dysplasia; HGD: High-grade dysplasia; sSM: Shallow submucosal invasive carcinoma; dSM: Deep submucosal invasive carcinoma; JNET: Japan Narrow-Band Imaging Expert Team; UCAN: Ulcerative colitis-associated neoplasms.

In the UCAN group, JNET type 2A and pit pattern type III/IV had a low PPV but with a high NPV in LGD diagnosis, and JNET type 2B and pit pattern type V₁ low irregularity had a low NPV in the diagnosis of HGD to sSM. This was because several lesions in UCAN were diagnosed as JNET type 2A or pit pattern type III/IV, even though they were actually HGD to sSM. Additional detailed analysis revealed that most endoscopists diagnosed about one-quarter of HGD to sSM lesions as JNET type 2A and one-third of HGD to sSM lesions as pit pattern type III/IV. Furthermore, a small number of dSM lesions were diagnosed as JNET type 2A or pit pattern type III/IV (Table 7).

In the SN group, JNET type 2A and pit pattern type III/IV had a high PPV but with a low NPV in LGD diagnosis, and JNET type 2B and pit pattern type V₁ low irregularity had a low PPV in the diagnosis of HGD to sSM. Because JNET type 2B and pit pattern type V₁ low irregularity include lesions from LGD to dSM, these types have low PPV even in non-UC patients[17,19,27]. Several LGD and dSM lesions in the SN group were diagnosed as JNET type 2B and pit pattern type V₁ low irregularity. JNET type 3 and pit pattern type V₁ high irregularity/V_N in both UCAN and SN groups showed low sensitivity but with high specificity and accuracy. Previous studies showed that JNET type 3 and pit pattern type V₁ high irregularity/V_N have high specificity for dSM diagnosis in both UC and non-UC patients[17-19,22]. Regardless of whether the surface and vascular patterns are modified by inflammation, JNET type 3 and pit pattern type V₁ high irregularity/V_N have been confirmed to be useful in diagnosing dSM among UC patients. In UCAN, the tumors' surface structure sometimes could not represent the dysplastic change due to the bottom-up growth pattern; hence, it is considered that several lesions are underestimated by endoscopic classifications. Additionally, SN located in the inflamed mucosa, especially SN in the severely inflamed mucosa, tends to be misdiagnosed due to the influence of inflammation.

Intra-observer agreement was higher among non-experts than among experts; however, the difference was not statistically significant. Inter-observer agreement did not also significantly differ but was higher in experts than in non-experts. Irrespective of the endoscopists' experience, a consistent endoscopic diagnosis of neoplastic lesions in UC patients was difficult to achieve. In particular, the intra- and inter-observer agreements were lower for UCAN than for SN.

The present study has some limitations. First, our study was conducted on a small number of cases; however, given its retrospective nature, the same size could not be set a priori. We believe that the small number of typical LGDs in this study was responsible for the unsatisfactory diagnostic accuracy. Second, only neoplastic lesions evaluated using both the JNET and pit pattern classifications were included. While inflammation and regenerative changes might be evaluated as neoplastic patterns by both JNET and pit pattern classifications, our study could not include non-neoplastic lesions. Non-neoplastic lesions should be included in future studies. Third, differentiation between UCAN and SN was based on pathology; nevertheless, even in pathology, distinguishing UCAN from SN can be difficult.

CONCLUSION

The JNET and pit pattern classifications did not show high accuracy in diagnosing the pathology and invasion depth of neoplastic lesions in UC patients. Overall, the endoscopic diagnosis of UCAN tended to be underestimated as compared to the pathological results. Endoscopic diagnosis of neoplastic lesions in UC patients is still difficult, and treatment strategies need to be carefully determined.

ARTICLE HIGHLIGHTS

Research background

Patients with long-standing ulcerative colitis (UC) have a risk of colorectal tumors due to chronic inflammation. Endoscopic treatments for patients with UC have gradually increased and have attracted attention recently.

Research motivation

Surface and vascular patterns of tumors located in the inflamed mucosa are likely to be modified by inflammation. For that reasons, it is unclear whether the Japan Narrow-Band Imaging Expert Team (JNET) classification and pit pattern classification are applicable to the diagnosis of neoplastic lesions in patients with UC.

Research objectives

The present study aimed to clarify the diagnostic performance of JNET and pit pattern classifications for neoplastic lesions in patients with UC.

Research methods

We analyzed 41 UC patients with 44 lesions that could be assessed using both the JNET and pit pattern classifications. We divided them into the UC-associated neoplasms (UCAN) group (21 lesions) and sporadic neoplasms (SN) group (23 lesions) according to the pathological results. Six endoscopists each evaluated the endoscopic findings by using both endoscopic classifications.

Research results

In the UCAN group, the accuracy of diagnosis for JNET types 2A, 2B, and 3 by experts was 90.5%, 71.4%, and 85.7%, respectively. In the same manner, the accuracy of diagnosis for pit pattern type III/IV, type V₁ low irregularity, and type V₁ high irregularity/V_N by experts was 85.7%, 57.1%, and 76.2%, respectively.

Research conclusions

The JNET and pit pattern classifications did not show high accuracy in diagnosing the pathology and invasion depth of neoplastic lesions in patients with UC. Endoscopic diagnosis of UCAN tended to be underestimated, as compared to the pathological results.

Research perspectives

Future prospective studies with a large number of UC patients are needed in clinical practice.

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FOOTNOTES

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