Magnifying Narrow Band Imaging (NBI) for the Diagnosis of Localized Colorectal Lesions Using the Japan NBI Expert Team (JNET) Classification

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Keywords

Narrow band imaging · Japan NBI Expert Team (JNET) classification · NBI International Colorectal Endoscopic (NICE) classification · Colorectal tumors · Magnifying endoscopy

Abstract

Objective: The Japan NBI Expert Team (JNET) proposed a new narrow band imaging (NBI) classification system for colorectal tumors in June 2014. In this classification system, types 1, 2A, 2B, and 3 correspond to hyperplastic polyps (HPs) including sessile serrated polyps (SSPs), low-grade dysplasia (LGD), high-grade dysplasia (HGD) to shallow submucosal invasive (SM-s) carcinomas, and deep submucosal invasive (SM-d) carcinomas, respectively. **Methods:** To validate this system, we performed a retrospective image evaluation study, in which 199 colorectal tumors previously assessed by NBI magnifying endoscopy were classified by 3 blinded experienced colonoscopists using the JNET system. The results

were compared with the final pathological diagnoses to determine the JNET classification's accuracy. The interobserver agreement was calculated, and the intraobserver agreement was assessed after 6 months. **Results:** The final pathological diagnoses identified 14 HPs/SSPs, 127 LGDs, 22 HGDs, 19 SM-s carcinomas, and 17 SM-d carcinomas. The respective sensitivities, specificities, positive predictive value, negative predictive value, and accuracies were as follows: Type 1, 85.7, 99.5, 92.3, 98.9, and 98.5%; Type 2A, 96.0, 81.9, 90.3, 92.1, and 90.9%; Type 2B, 75.6%, 90.5, 67.3, 93.4, and 87.4%; and Type 3, 29.4%, 100, 100, 93.8, and 94.0%. The interobserver agreement and the intraobserver agreement were moderate (κ value: 0.52) and excellent (κ value: 0.88), respectively. Lesions presenting as Type 2B during NBI comprised a range of colorectal tumors, including HGDs, SM-s, and SM-d. **Conclusions:** The JNET classification was useful for the diagnosis of HPs/SSPs, LGDs, and SM-d, but not SM-s lesions. For low-confidence cases, magnified chromoendoscopy is recommended to ensure correct diagnoses.

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Introduction

Narrow band imaging (NBI), which visualizes vessel and surface patterns in detail, is generally considered to provide useful diagnostic information about gastrointestinal lesions identified via endoscopy [1]. Several studies have indicated that NBI observations of colorectal polyps are very useful, accurate predictors of histology [2–6]. Although previous studies [2–6] addressed the utility of NBI observations (i.e., vascular and surface patterns) for the endoscopic diagnosis of colorectal tumors, a universal definitive classification system has not yet been established. The NBI International Colorectal Endoscopic (NICE) classification, published by the Colon Tumor NBI Interest Group (CTNIG), uses the colors, vessels, and surface patterns observed during endoscopy to classify the results of nonmagnifying evaluations [7, 8]. However, colonoscopists often encounter difficulties with cases classified as NICE Type 2, as this category includes a variety of pathologies ranging from low-grade dysplasia (LGD) to shallow submucosal invasive cancer (SM-s) [9, 10]; the former is suitable for endoscopic mucosal resection (EMR), whereas the latter is indicated for endoscopic submucosal dissection (ESD) [11].

The Japan NBI Expert Team (JNET), which comprises 38 members specialized in colonoscopy, attempted to establish a new NBI classification system for colorectal tumor diagnosis that would overcome the limitations of the NICE classification system. This novel NBI magnifying classification system for colorectal tumors, the JNET classification, was proposed in June 2014 [11]. The JNET classification uses magnifying NBI observations with a focus on vessel and surface patterns to diagnose colorectal tumors as Types 1, 2A, 2B, and 3. Type 1 is characterized by an invisible vessel pattern and a surface pattern comprising dark and white spots, similar to the surrounding normal mucosa. Type 2A is defined as vessels of a regular caliber and distribution (meshed/spiral pattern) and a regular (tubular/branched/papillary) surface pattern. Type 2B is defined as vessels with a variable caliber and irregular distribution and an obscure surface pattern. Type 3 is characterized as a vessel pattern comprising areas of loose or interrupted thick vessels and a surface pattern of amorphous areas (Fig. 1). Types 1, 2A, 2B, and 3 correlate with the pathological diagnoses of hyperplastic polyp (HP) and sessile serrated polyp (SSP), LGD, high-grade dysplasia (HGD) and SM-s cancer (T1a; <1,000 μ m), and deep submucosal invasive cancer (SM-d: T1b; $\geq$ 1000 μ m), respectively [11]. The NICE and JNET classifications differ most significantly in that Type 2 from

the former is subdivided into Types 2A and 2B in the latter, thus allowing the discrimination of LGD and HGD-SM-s lesions. To evaluate the usefulness of the JNET classification, we conducted a retrospective study to evaluate the interobserver and intraobserver agreement among 3 observers and, thus, determine the usefulness of the JNET classification.

Methods

Study Design

We conducted a retrospective image evaluation study of digital files containing endoscopic images of localized colorectal neoplastic lesions that had been treated with EMR, ESD, or surgical operation from April 2010 to April 2015. Endoscopic images were taken using magnified NBI. The exclusion criteria were advanced colorectal adenocarcinoma, neoplastic lesions associated with inflammatory bowel disease, and polyposis. In addition, colorectal tumors >5 cm were excluded from this study because a precise NBI diagnosis is difficult in such cases. A total of 199 lesions were randomly selected from among 510 colorectal neoplastic lesions subjected to NBI observation at Kindai University Hospital. Per lesion, 1–4 representative NBI magnifying endoscopy images were selected by Y.K. and 3 other observers (H.K., T.S., and Y.A.) who were blinded to the pathological, white light, and chromoendoscopic findings and the clinical information. The 199 lesions were classified according to the JNET system and evaluated by the 3 observers. All evaluated images were obtained via magnifying colonoscopy (device: CF-H260AZI, PCF-260AZI; Olympus Optical Co., Tokyo, Japan).

Initially, the 3 experienced colonoscopists (H.K., T.S., and Y.A.; NBI diagnosis >1,000 cases over >5 years) independently diagnosed the images obtained from the 199 cases. If the individual diagnostic interpretations differed, the 3 reviewers discussed the case until a consensus was obtained. For cases in which a diagnosis of JNET classification was difficult because of inconsistent interpretations between the vessel and surface patterns, the 3 reviewers determined the final JNET diagnosis via consensus after discussion. The consensus NBI diagnosis was then compared with the final pathological diagnosis. Histological diagnoses were reviewed by a pathologist (T.T.) with expertise in the field of colorectal tumors and blinded to the NBI findings. Histopathology was defined according to the World Health Organization classification system [12]. Initially, the interobserver agreement among the 3 observers was calculated. Six months later, the intraobserver agreement was calculated for a single observer (H.K.).

Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated for each classification category. The interobserver agreement and the intraobserver agreement were calculated using κ coefficients, using the following arbitrary interpretation reported by Landis and Koch [13]: poor, 0–0.20; fair, 0.21–0.40; moderate, 0.41–0.60; substantial, 0.61–0.80; and excellent, 0.81–1.00.

	Type 1	Type 2A	Type 2B	Type 3
Vessel pattern	Invisible ¹	Regular caliber ² Regular distribution (meshed/spiral pattern)	Variable caliber Irregular distribution	Loose vessel areas Interruption of thick vessels
Surface pattern	Regular dark or white spots Similar to surrounding normal mucosa	Regular (tubular/branched/papillary)	Irregular or obscure	Amorphous area
Most likely histology	Hyperplastic polyp/ Sessile serrated polyp	Low-grade dysplasia	High-grade dysplasia/ Shallow submucosal invasive cancer ³	Deep submucosal invasive cancer
Endoscopic image

Fig. 1. The Japan Narrow Band Imaging (NBI) Expert Team (JNET) classification. ¹ If visible, the caliber in the lesion is similar to that of the surrounding normal mucosa. ² Microvessels are often distributed in a punctate pattern, and well-ordered reticular or spiral vessels may not be observed in depressed lesions. ³ Deep submucosal invasive cancer may be included. The NBI images corresponding to each JNET type were obtained from patients recruited for this study.

Table 1. The relationship between JNET classification and histology

JNET classification	Histology				
	HP/SSP	LGD	HGD	SM-s	SM-d
Type 1 (<i>n</i> = 13)	12 (92.3)	1 (7.7)			
Type 2A (<i>n</i> = 135)	2 (1.5)	122 (90.4)	8 (5.9)	2 (1.5)	1 (0.7)
Type 2B (<i>n</i> = 46)		4 (8.7)	14 (30.4)	17 (37.0)	11 (23.9)
Type 3 (<i>n</i> = 5)					5 (100)

HP, hyperplastic polyp; SSP, sessile serrated polyp; LGD, low-grade dysplasia; HGD, high-grade dysplasia; SM-s (T1a), shallow submucosal invasive cancer; SM-d (T1b), deep submucosal invasive cancer.

Results

JNET Classification

As shown in Figure 1, all 199 colorectal tumors enrolled in this study were classified as JNET Type 1, Type 2A, Type 2B, or Type 3, as has been previously described [11]. Representative NBI pictures from this study that correspond to each JNET type are shown in Figure 1.

Sensitivity, Specificity, PPV, NPV, and Accuracy of JNET

The pathological analysis of 199 lesions revealed 14 cases of HP/SSP, 127 cases of LGD, 22 cases of HGD, 19 cases of SM-s, and 17 cases of SM-d. Table 1 demonstrates the relationships between JNET categories and histology, whereas Table 2 presents the diagnostic characteristics for each category. The sensitivity, specificity, PPV, NPV, and accuracy for Type 1 were 85.7% (12/14), 99.5% (184/185),

Table 2. Performance characteristics (95% CI) of each type in JNET classification

	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
Type 1	85.7 (57.2–98.2)	99.5 (97.0–100.0)	92.3 (64.0–99.8)	98.9 (64.0–99.8)	98.5 (95.7–99.7)
Type 2A	96.0 (91.0–98.7)	81.9 (71.1–90.0)	90.3 (84.1–94.8)	92.1 (82.7–97.4)	90.9 (86.1–94.6)
Type 2B	75.6 (59.7–87.6)	90.5 (84.8–94.6)	67.3 (52.0–80.5)	93.4 (88.3–96.8)	87.4 (82.0–91.7)
Type 3	29.4 (10.3–56.0)	100 (98.0–100)	100 (47.8–100)	93.8 (89.4–96.8)	94.0 (89.7–96.8)

CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

92.3% (12/13), 98.9% (184/186), and 98.5% (196/199), respectively. The corresponding values for Type 2A were 96.0% (122/127), 81.9% (59/72), 90.3% (122/135), 92.1% (59/64), and 90.9% (181/199), respectively; for Type 2B 75.6% (31/41), 90.5% (143/153), 67.3% (143/153), 93.4% (143/153), and 87.4% (174/199), respectively; and for Type 3 29.4% (5/17), 100% (182/182), 100% (5/5), 93.8% (182/194), and 94.0% (187/199), respectively.

Interobserver and Intraobserver Agreement for the JNET Classification

Moderate interobserver agreement was observed among the 3 observers (vessel/surface pattern κ values = 0.52/0.52). The complete concordance rate for vessel and surface patterns among the 3 observers was 67%. In contrast, the intraobserver agreement was excellent (vessel/surface pattern κ values = 0.87/0.88).

Discussion

In this study, we obtained preliminary data regarding the clinical utility of the JNET classification system for the diagnosis of colorectal tumors by classifying 199 colorectal lesions through a review of magnifying NBI images and a comparison with pathological findings. The NBI diagnoses of JNET Type 1 and Type 2A correlated strongly with the HP-SSP and LGD types, respectively, suggesting that these lesion types could be diagnosed using the JNET classification alone. In contrast, pathological examination revealed that JNET Type 2B included a wide variety of colorectal tumors ranging from LGD to SM-d lesions. Therefore, a careful consideration of the endoscopic treatment strategy would be required for a diagnosed JNET Type 2B lesion. Similarly, the diagnosis of SM-d lesions according to the JNET classification alone was not satisfactory, as these lesions could be classified as either JNET Type 3 or Type 2B. Conversely, JNET Type 3 cor-

related strongly with SM-d lesions. Taken together, these data suggest that the JNET classification system is a useful tool for the diagnosis of HP-SSP, LGD, and SM-d lesions.

Consistent with a previous report by Sumimoto et al. [14], the sensitivity, specificity, PPV, NPV, and accuracy of the JNET Type 1 classification were satisfactory. These parameters were similarly high for JNET Type 2A, suggesting that HP-SSP and LGD lesions can be accurately diagnosed using the JNET classification alone. The specificity and PPV of the JNET Type 3 classification were both 100%, indicating that JNET Type 3 correlates with the pathological diagnosis of SM-d lesions that require surgical resection. In contrast, the sensitivity, specificity, PPV, NPV, and accuracy were unsatisfactory for Type 2B lesions, as pathological analysis revealed that this category included various types of colorectal tumors while excluding HP/SSP lesions. Therefore, subsequent magnifying chromoendoscopy is strongly recommended for lesions within this category.

Studies have been performed to evaluate the usefulness of the NICE classification for the diagnosis of colorectal tumors since its initial proposal in 2009 [7, 8]. Hattori et al. [9] reported that the risk of failure to detect diminutive and small colorectal invasive cancers using the “resect and discard” strategy might be avoided by using the NICE classification. In another multicenter study, Rees et al. [10] provided evidence that an NBI-assisted optical diagnosis could not currently be recommended for the diagnosis of colorectal polyps in the absence of NBI expertise. These negative findings might be attributable to the inclusion of a wide range of pathologies (from LGD to SM-s [T1a]) within the NICE Type 2 classification.

Therefore, colonoscopists have often encountered difficulties regarding the application of NICE classifications to the endoscopic diagnosis of colorectal tumors, including difficulties regarding the selection of an appropriate endoscopic resection procedure (i.e., choosing between EMR, which is mainly intended for LGD and HGD le-

Fig. 2. A therapeutic strategy based on the JNET classification and magnifying chromoendoscopy.

sions, and ESD, which is intended for lesions from HGD to SM-s [T1a]). The JNET classification, which includes NBI magnifying observations, was proposed to resolve these problems. The use of magnifying endoscopy to subdivide the NICE Type 2 category into the JNET Type 2A and Type 2B categories promoted the diagnosis of LGD lesions in both the present study and a previous study [11]. It should be noted, however, that the diagnostic value of the JNET classification is unsatisfactory, especially regarding JNET Type 2A and 2B. Therefore, it is too early to determine the superiority of the JNET classification over the NICE classification until the results of clinical trials that directly address the utilities and accuracies of both classifications are available.

Consistent with the previous study [11], our results support the superiority of the JNET classification over the NICE classification. The utilization of magnifying NBI might partially explain the improved diagnostic accuracy of the JNET classification for LGD lesions. Magnifying endoscopy can optically zoom up to 100 times in real time and reveal detailed pit pattern characteristics, compared with the conventional observations used to differentiate between non-neoplastic polyps and neoplastic colorectal polyps [15, 16].

To our knowledge, this is the first study to demonstrate interobserver and intraobserver colorectal tumor diagnosis agreement regarding the JNET classification.

Although the interobserver agreement was moderate, the intraobserver agreement was excellent. This might be because a significant proportion of JNET Type 2A and Type 2B lesions comprise uncertain or borderline lesions, leading to highly variable diagnoses. The presence of Type 2A–2B borderline lesions might affect not only the interobserver agreement, but also the specificity and sensitivity. Therefore, it was difficult to definitively diagnose a significant proportion of colorectal tumors in this study as Type 2A or Type 2B, which may contribute to the low specificity of Type 2A. The high sensitivities of JNET Type 1 and Type 2A in this study suggest that these types correlate strongly with HP-SSP and LGD, respectively, and can, therefore, be used alone to diagnose these lesions. In contrast, the pathological examination revealed that JNET Type 2B included a wide variety of colorectal tumors, and, therefore, could not specifically indicate HGD or SM-d. Similarly, the diagnosis of SM-d lesions using the JNET classification alone was unsatisfactory, as these lesions exhibit characteristics of both Type 3 and Type 2B. However, JNET Type 3 correlated strongly with SM-d lesions. Taken together, these data suggest that the JNET classification system is a useful tool for the diagnosis of HP/SSP, LGD, and SM-d lesions.

JNET Type 2A and Type 2B had a relatively low specificity and sensitivity, respectively. We attribute this to the fact that JNET Type 2B lesions comprise a variety of colorectal tumors and that a significant proportion of colorectal tumors exhibit Type 2A–2B borderline NBI findings. Therefore, colonoscopists should perform magnifying chromoendoscopy followed by a pit pattern diagnosis for these uncertain 2A–2B borderline lesions. Based on the findings presented in this study, we have devised a flowchart of our strategy, for the selection of endoscopic colorectal tumor treatment, which employs both the JNET classification and chromoendoscopy (Fig. 2).

It should be noted that prospective and multicenter studies that address the usefulness of both the JNET classification and magnifying chromoendoscopy for the diagnosis of colorectal tumors will be required to confirm this concept.

This study has some notable limitations. First, the study was conducted using pre-existing digital image files from medical records. Second, it was conducted at a single center, and JNET classification was performed only by expert colonoscopists. Third, only a few JNET Type 3 cases were included. Finally, this study did not include a comparison with other classification systems, such as the Sano, Hiroshima, Showa, and Jikei classifications [17–20].

In conclusion, the JNET classification is a valid tool for predicting the histology of localized colorectal lesions. A JNET diagnosis of Type 1, 2A, or 3 corresponds to a pathological diagnosis of a HP/SSP, LGD, or SM-d lesion, respectively, without requiring magnifying chromoendoscopy. However, magnifying chromoendoscopy is strongly recommended for the accurate diagnosis of Type 2B and uncertain 2A–2B borderline lesions. Multicenter prospective studies to validate our conclusions should be conducted in the near future.

Statement of Ethics

Ethical permission for this study was granted by the Review Board of the Kindai University Hospital (approval No. 28-220). The procedures followed were in accordance with the guidelines of the World Medical Association's Declaration of Helsinki (1964, and its later amendments).

Disclosure Statement

The authors have no conflicts of interest to declare.

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