Utility of Japan Narrow Band Imaging Expert Team Classification Using Narrow Band Imaging for Evaluation of Colonic Polyps

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Abstract

Background Narrow band imaging (NBI) is an advanced endoscopic imaging technique that enhances visualization of the mucosal surface and is used as a screening tool for colonic polyps. Its usefulness is currently explored to a lesser extent in India. So, we assessed the utility of Japan NBI Expert Team (JNET) classification for characterization of colorectal polyps.

Methods A prospective observational study was performed from January 2018 to June 2019 of patients undergoing colonoscopy at a tertiary care hospital. NBI image of polyps was captured followed by either polypectomy/biopsy. Histopathology results were correlated with the pattern revealed by NBI on polyps using the JNET classification.

Results A total of 80 patients, 61 (76.25%) male with a mean (standard deviation [SD]) age of 58.41 ± 14.59 years were included. Out of the 90 lesions, 23 (25.5%) had type-1 pattern, 45 (50%) had 2A, 13 (14.4%) had 2B, and 9 (10%) had type-3 pattern. On histopathology, majority 51 (59.3%) were found to be adenomatous with low-grade intramucosal neoplasia. When correlating our results with JNET category type 1 and hyperplastic polyps, the sensitivity was 90%, specificity was 97%, negative predictive value was 97%, positive predictive value was 90%, and diagnostic accuracy was 96%. Correlating type 2A and low-grade intramucosal neoplasia had results of 78, 87, 76, 90, and 82%, respectively. Correlating type 2B and high-grade intramucosal neoplasia had results of 83, 90, 99, 38, and 90%, respectively. Correlating type 3 and deep submucosal cancer had results of 88, 98, 99, 78, and 97%, respectively.

Conclusion NBI shows excellent probability to exclude carcinoma possibilities based on the changes in colonic mucosal features. Owing to slightly lower sensitivity for type 2B, it needs additional investigation using pit pattern diagnosis. We demonstrated the high-diagnostic performance of NBI in making an accurate diagnosis of early colorectal cancers in colonoscopy. Further refinement in the NBI technology might add to the current evidence for characterization of polyps.

Keywords

- narrow-band imaging
- colonic polyps
- surface pattern
- vessel pattern

Introduction

Colonic polyps are overgrowths of the colonic mucosa which carry a low risk of becoming malignant and are often encountered during routine standard screening procedures.¹

Screening helps to detect polyps which can turn malignant in people who have no symptoms of the disease.² Colorectal cancer (CRC) is life-threatening when diagnosed in advanced stages.³ Most commonly used screening tool for CRC is colonoscopy. Colonoscopic detection and polypectomy

represents the most important prevention method for CRC.⁴ The prevalence of adenoma is approximately 10% in sigmoidoscopy and >25% in colonoscopy, whereas the prevalence of CRC among these is <1%.⁵ The standard colonoscopic procedure uses magnifying chromoendoscopy principle. Narrow-band imaging (NBI; Olympus, Japan) was introduced in 1999 and uses optical technology for enhanced images and surface patterns of lesions resulting in better outcomes in terms of detection and early diagnosis of colorectal tumors.⁶ NBI, when combined with magnification colonoscopy, is useful for histological prediction, or for estimating the depth of invasion.⁷ NBI with magnification is useful in differentiating neoplastic from nonneoplastic lesions. Several magnifying NBI classifications for diagnoses of colorectal lesions are developed.⁸⁻¹¹ Of late, Japan NBI Expert Team (JNET) classification was developed.¹² But its usefulness in Indian patients is unexplored. So, we aim to study the diagnostic accuracy of the JNET classification and correlate histopathology results with the pattern revealed by NBI in a prospective manner.

Methods

A prospective observational study was performed from January 2018 to June 2019 of patients undergoing colonoscopy at a super specialty Gastroenterology outpatient and inpatient department of a tertiary care teaching hospital. Inclusion criteria were consecutive patients of either sex of any age group who underwent elective colonoscopy for screening, surveillance or evaluation of symptoms. Patients found to have polyps with white light were followed by subsequent NBI. Exclusion criteria were patients' already diagnosed with colorectal neoplasm, colectomy, polyposis syndrome, past history of Inflammatory Bowel Disease (IBD) with pseudopolyps, and pregnancy. Ethical approval was obtained from institutional ethics committee. Written informed consent was also obtained from all patients prior to the start of study.

Colonoscope (CFQ-180AL, Olympus, Tokyo, Japan) was used for the examination. Each polyp detected was washed free of stool and mucus, and then examined under NBI without magnification. NBI image of polyps was captured followed by either polypectomy or biopsies. Histopathology of biopsy sample was correlated with pattern revealed by NBI on polyps using JNET classification. Data were recorded on a predesigned proforma and real time data entry was done on Microsoft excel for windows. Endoscopic diagnosis was done using JNET classification. JNET types 1, 2A, 2B, and 3 correspond to the histopathological classifications of hyperplastic polyp (HP)/SSP, low-grade intramucosal neoplasia (LGN), high-grade intramucosal neoplasia (HGN)/shallow submucosal (SM-s) invasive cancer, and deep SM (SM-d) invasive cancer, respectively.

Patient Preparation

An electrolyte-balanced solution (polyethylene glycol) was prescribed to patients to be taken in 2 to 3 L of water in morning (5–7 a.m.). Patients were asked to drink this preparation every 15 to 20 minutes until the bowel's output was

clear or the solution was completely consumed. Colonoscopy was ideally performed between 10 a.m. to 2 p.m.

Histopathology Examination

Specimens were fixed in 20% formalin and histologically examined after hematoxylin and eosin staining. Histologic diagnosis was made by a pathologist blinded to the colonoscopic diagnosis at each step.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software for windows (v. 21, SPSS, Inc., Chicago, Illinois, United States). 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.

- Poor: 0 to 0.20.
- Fair: 0.21 to 0.40.
- Moderate: 0.41 to 0.60.
- Substantial: 0.61 to 0.80.
- Excellent: 0.81 to 1.00.

The criterion standard for validation of predictions was the histology of colorectal lesions.

Results

A total of 80 patients were studied with NBI and histopathology and 90 polyps were identified. There was male predominance 61 (76.25%) with a mean (standard deviation [SD]) age of 58.41 ± 14.59 years. The most common symptom at presentation was abdominal pain in 24 (30%) patients and comorbidity was diabetes mellitus in 21 (23.3%) patients. Demographic characteristics of patients are given in ►Table 1. Most of the polyps were seen in left-sided colon 55 (61.1%). The mean (SD) size of polyps was 1.32 ± 1.05 cm. Polyp of size >1 cm were seen in 61 (67.77%) cases. According to Paris classification majority were sessile 62 (68.8%) in nature. Out of the 90 lesions, 23 (25.5%) had type-1 pattern, 45 (50%) had 2A, 13 (14.4%) had 2B, and 9 (10%) had type-3 pattern. On histopathology, majority 51 (59.3%) were found to be adenomatous with low grade intramucosal neoplasia (►Table 2).

When correlating our results with JNET category type 1 (►Fig. 1A) and HPs (►Fig. 1B), the sensitivity was found to be 90%, specificity was 97%, NPV of 97%, PPV of 90%, and diagnostic accuracy was 96%. Correlating type 2A (►Fig. 2A) and low-grade intramucosal neoplasia (►Fig. 2B) had results of 78, 87, 76, 90, and 82%, respectively. Correlating type 2B (►Fig. 3A) and high-grade intramucosal neoplasia (►Fig. 3B) had results of 83, 90, 99, 38, and 90%, respectively. Correlating type 3 (►Fig. 4A) and SM-d cancer (►Fig. 4B) had results of 88, 98, 99, 78, and 97%, respectively (►Table 3). The relationship between JNET classification and histology is given in ►Table 4. In this study, the interobserver agreement was seen among

Table 1 Patient demographics

Patient characteristics	n (%)
Total no. of patients n (%)	80 (100)
Total no. of lesions	90
Mean $\pm$ SD (y)	58.41 $\pm$ 14.59
Male	61 (76.2)
M:F	3.2:1
Comorbidities, n (%)	
Diabetes mellitus	21 (23.3)
Hypertension	15 (16.7)
Ischemic heart disease	9 (10)
Cirrhosis of liver	3 (3.3)
Carcinoma	3 (3.3)
Cerebrovascular accident	2 (2.2)
Chronic kidney disease	2 (2.2)
Iron deficiency anemia	2 (2.2)
Immune thrombocytopenic purpura	1 (1.1)
Abdominal Koch's	1 (1.1)
Presenting symptom	
Abdominal pain	24 (30)
Chronic constipation	22 (27.5)
Chronic diarrhea	19 (23.7)
Weight loss	18 (22.5)
Blood in stool	11 (13.7)
Anemia	9 (11.2)
Melena	7 (8.7)
Perianal pain	5 (6.2)
Mucus in stool	2 (2.5)
Labial pigmentation	1 (1.2)
Clinical examination	
Left iliac fossa tenderness	14 (17.5)
Painful per rectal examination	6 (7.5)
Right iliac fossa tenderness	6 (7.5)
Epigastric tenderness	3 (3.7)
Pallor	2 (2.5)
Ascites	1 (1.2)
Hypogastrium tenderness	1 (1.2)

Abbreviations: F, female; M, male; SD, standard deviation.

the two observers, as kappa values = 0.76 which suggests substantial agreement (**Table 5**). In contrast, the intraobserver agreement was excellent, as kappa values = 0.93.

Discussion

By prospectively enrolling patients over 18 months' period in this observational study, we studied the utility of JNET classification for evaluation of colonic polyps and HP results were correlated with the pattern revealed by NBI. We demonstrated the high-diagnostic performance of NBI in making

Table 2 Polyp characteristics along with NBI features

Patient characteristics	n (%)
Site of polyp	
Ascending colon	22 (24.4)
Sigmoid	21 (23.3)
Rectum	17 (18.8)
Descending colon	15 (16.6)
Transverse colon	5 (5.5)
Throughout colon	5 (5.5)
Cecum	2 (2.2)
Splenic flexure	2 (2.2)
Hepatic flexure	1 (1.1)
Distribution of polyp in colon	
Left sided colon	55 (61.1)
Right sided colon	30 (33.3)
Throughout colon	5 (5.5)
Polyp morphology	
Sessile	62 (68.9)
Pedunculated	17 (18.9)
Flat	11 (12.2)
Polyp size (Mean $\pm$ SD) cm	1.32 $\pm$ 1.05
Polyp size (cm)	
>1	61 (67.8)
<0.5	23 (25.5)
0.6–0.9	6 (6.7)
NBI as per JNET classification	
Type 1	23 (25.6)
Type 2A	45 (50)
Type 2B	13 (14.4)
Type 3	9 (10)
Histopathology	
Hyperplastic	21 (24.4)
Low-grade intra-mucosal neoplasia (adenomatous)	51 (59.3)
High-grade intramucosal neoplasia	6 (7)
Deep submucosal invasive cancer	8 (9.3)

Abbreviations: JNET, Japan NBI expert team; NBI, narrow band imaging; SD, standard deviation.

an accurate diagnosis of early colorectal cancers in colonoscopy. In the present study, majority of the patients were in the age group of 61 to 70 years. Older age appears to have a positive correlation with an increased development of HPs as seen evidently from studies conducted across the world.^{13,14} Another risk factor that differs between serrated colorectal polyps and sessile serrated adenoma or polyp in comparison to conventional adenomas is male sex.¹⁵ While males clearly have a higher risk of conventional adenomas compared with

Fig. 1 (A) Vessel pattern is regular, surface pattern is dark and white spot similar to normal mucosa, (×magnification). (B) The crypt lining is irregular, along the surface, deeper down crypts are uniform, mild increase in mononuclear inflammation in lamina propria, histopathology (hematoxylin and eosin stain, ×200 magnification). NBI, narrow band imaging.

Fig. 2 (A) Vessel pattern is regular distribution and caliber, surface pattern- regular tubular pattern. (×magnification). (B) Surface is tubulovillous configuration, lamina propria contains crowded crypts lined by columnar epithelium with nuclear stratification confined to basal half of cell, (hematoxylin and eosin stain, ×200 magnification). NBI, narrow band imaging.

Fig. 3 (A) Vessel pattern is variable pattern and irregular distribution, surface is irregular and obscure. (×2 magnification). (B) Crypts are crowded, architecture irregularly, cribriforming, nuclei are oval to elongated, stratified and atypical with hypochromasia, (hematoxylin and eosin stain, ×400 magnification). NBI, narrow band imaging.

Fig. 4 (A) Vessel pattern—loose vessel area, interruption of thick vessel, amorphous surface pattern, (×magnification). (B) Atypical glands aligned by hyperchromasia, round to oval nuclei with columnar cell, infiltration gland with desmoplastic stroma, (hematoxylin and eosin stain, ×200 magnification). NBI, narrow band imaging.

Table 3 Characteristics (95% CI) of each type in JNET classification

JNET class	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %
Type 1	90 (71.09–97.35)	97 (90.03–99.2)	90 (90.03–99.2)	97 (71.09–97.35)	96 (89.12–98.26)
Type 2A	78 (65.37–87.51)	87 (73.29–94.4)	90 (61.33–85.76)	76 (76.5–95.16)	82 (73.06–88.75)
Type 2B	83 (43.65–96.99)	90 (82.32–95.09)	38 (93–99.77)	99 (17.71–64.48)	90 (82.08–94.65)
Type 3	88 (52.91–97.76)	98 (91.54–99.33)	78 (93.33–99.78)	99 (45.26–93.68)	97 (90.65–98.86)

Abbreviations: CI, confidence interval; JNET, Japan NBI (narrow band imaging) expert team; NPV, negative predictive value; PPV, positive predictive value.

females, the same is not true for serrated colorectal polyps and sessile serrated adenoma or polyp; females are at equal or slightly higher risk of harboring these lesions.¹⁶ In our study, we had male predominance with 61 (76.25%), with a male-to-female ratio of 3.2:1, respectively. Similar trend was seen in multiple other studies.^{15,16} Diabetes has been shown to be a risk factor for adenomas in some studies.¹⁷ Diabetes mellitus was the most common comorbidity seen in 21 (23.3%) of the patients with polyps.

In a German study in 2007 with 90 patients, 102 (51%) of polyps were seen in the right colon, 69 (34.5%) in the left colon, and 29 (14.5%) in the rectum.¹⁸ In a Japanese study in 2010 with 127 patients, 81 (62.3%) lesions were located in the left colon and rectum and 49 (37.7%) lesions were located in the right and transverse colon.¹⁹ Our study had similar findings; most of the polyps were located in the left sided colon and rectum, 55 (61.1%) as compared with right sided colon 30 (33.3%). One needs to visualize the mucosa of left-sided colon and rectum with proper magnification since chances of finding these lesions are prominent in these areas. The mean size of the polyps was found to be 9.9 mm (range: 2–50 mm)¹⁸ in 90 patients, while it was 17 mm (range: 5–80 mm) with 127 patients in the Japanese study.¹⁹ Our findings are in line with these as the mean size of polyps in the present study was 1.32 ± 1.05 cm.

Morphologically, characterization of polyp is usually done with the Paris classification for gastrointestinal polyps.²⁰

Polypoid lesions (Paris 0–I), sessile or pedunculated polyps (>10 mm), have a low-invasive potential (7%), whereas as those with a depressed component (either Paris IIc or IIa + c) have a 31% risk of SM invasion.²¹ In this study, according to Paris classification most of the polyps found were sessile 62 (68.89%), other lesions were pedunculated 17 (18.89%) and flat type in 11 (12.22%) cases.

In the present study, pathological analysis of 90 lesions revealed cases of HP as 21 (24.4%), 51 (59.3%) cases of low-grade dysplasia (LGD), 6 (7%) cases of high-grade dysplasia (HGD) and 8 (9.3%) cases of SM-d invasion. In a Japanese study (2010), 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.²² The present study contained 23 patients with type-1 patterns, out of which 21 (91.3%) patients had HPs on histology and other two lesions were nonhyperplastic. The actual correlation between type 1 and HPs was seen only in 19 patients, with a sensitivity of 90%, specificity of 97%, and diagnostic accuracy of 96%. Type-2A patterns demonstrated in this study by 45 patients, but according to histopathology low-grade intramucosal adenoma was found in 51 lesions. Out of 45 lesions with type 2A, only 40 lesions had actual correlation with histology of low-grade intramucosal adenoma, rest of the five lesions could not be identified as having low-grade intramucosal adenoma.

Table 4 Relationship between JNET classification and histology

JNET Class	Histology				Other
	HP	LGD	HGD	SM-d	
Type 1 (n = 23)	19 (82.6%)	2 (8.7%)	0	0	2 (8.7%)
Type 2A (n = 45)	2 (4%)	40 (88%)	1 (2%)	1 (2%)	1 (2%)
Type 2B (n = 13)	0	8 (61%)	5 (46.1)	0	0
Type 3 (n = 9)	0	1 (1.1%)	0	7 (77%)	1 (1.1%)

Abbreviations: HGD, high-grade dysplasia; HP, hyperplastic polyp; JNET, Japan NBI (narrow band imaging) expert team; LGD, low-grade dysplasia; SM-d, deep submucosal invasive cancer.

Table 5 Interobserver agreement for JNET classification

Rater 1		Rater-2				Total
		Type 1	Type 2A	Type 2B	Type 3	
Type 1	No.	20	3	0	0	23
	%	87.00	7.00	0.00	0.00	25.60
Type 2A	No.	3	38	4	0	45
	%	13.00	88.40	23.50	0.00	50.00
Type 2B	No.	0	2	11	0	13
	%	0.00	4.70	64.70	0.00	14.40
Type 3	No.	0	0	2	7	9
	%	0.00	0.00	11.80	100.00	10.00
Total	No.	23	43	17	7	90
	%	100.00	100.00	100.00	100.00	100.00
Symmetric measures		Value	Asymp. SE	Approx. T ^b	Approx. Sig.	
Measure of agreement	Kappa	0.765	0.058	11.394	0	
No. of valid cases		90				

Abbreviations: Approx., approximately; Asymp., asymptomatic; JNET, Japan NBI (narrow band imaging) expert team; SE, standard error; T^b, using the asymptotic standard error assuming the null hypothesis.

Note: not assuming the null hypothesis.

Using the asymptotic standard error assuming the null hypothesis.

In a recent study of Sumimoto et al,²³ with 2,933 lesions, the specificity of type 2B was found to be 82.8% and PPV of type 2B was 50.9%, significantly lower than those of the other type of JNET. The ability of type 2B to identify HGD or SM carcinoma was not significant. These results are somewhat in line with our findings which does not show any significant correlation between type 2B (►Fig. 2A) and HGD (►Fig. 2B) as specificity was 90% and PPV was 38%. This may be contributed to type 2B pattern, which shows various histological findings, ranging from LGD to SM-d carcinoma.

The type-2B pattern was found in 13 (14.4%) patients, with distributions of 5 lesions with high-grade intramucosal hyperplasia, 7 lesions with low-grade intramucosal neoplasia, and 1 lesion with deep SM cancer with histopathology. Actual correlation between type-2B (►Fig. 3A) and high-grade intramucosal dysplasia (►Fig. 3B) was found only in five patients with a sensitivity of 83%, specificity of 90%, and accuracy of 90%.

JNET type 3 showed specificity of 98% and diagnostic accuracy of 97%. The type-3 pattern detected in nine lesions,

out of this seven came out to be SM-d cancer and 2 with non-cancerous. Correlation of type 3 and SM-d cancer was seen in 7 lesions only with a sensitivity of 88%, specificity of 98%, and diagnostic accuracy of 97%, indicating that JNET type 3 correlated with the pathological diagnosis of SM-d lesions that require surgical resection.

In a Japanese study, moderate interobserver agreement was observed among the three observers (vessel/surface pattern κ values = 0.52/0.52). The complete concordance rate for vessel and surface patterns among the three observers was 67%. In contrast, the intraobserver agreement was excellent (vessel/surface pattern κ values = 0.87/0.88).²² In this study, interobserver agreement was observed among the two observers, as kappa values = 0.76 which suggest substantial agreement. In contrast, the intraobserver agreement was excellent, as kappa values = 0.93. A recent meta-analysis of RCT in 2019, included 11 trials comprising 4,491 patients and 6,636 polyps that fit their criteria. Adenomas were detected in a higher percentage of patients examined with NBI compared with WLE (45.2 vs. 42.3%; odds ratio [OR] = 1.14; 95%

confidence interval [CI]: 1.01–1.29). The effect of NBI on adenoma detection was much greater when patient bowel preparation could be described as “best” (OR = 1.3; 95% CI: 1.04–1.62) compared with when it was categorized as just “adequate” (OR = 1.07; 95% CI: 0.92–1.24). NBI was also more successful at detecting nonadenomatous polyps (OR = 1.24; 95% CI: 1.06–1.44) and flat polyps (OR = 1.24; 95% CI: 1.02–1.51) compared with white light endoscopy (WLE).²⁴

Limitations

When interpreting the results from our study, one needs to keep in mind its limitations. This was a single centered study with a small sample size of approximately 80 patients. This study was conducted in a tertiary referral center and would have thus included a select set of patients due to a referral bias, the results of which may not be generalizable outside of this environment. This was an uncontrolled study, and the number of detected cancers was small. Therefore, in the near future we need to compare the diagnostic performance of magnification NBI with other conventional endoscopy methods (e.g., chromoendoscopy) dealing with a substantial number of early colorectal cancer cases. Low magnification was used in our study which appears a major limitation since high magnification was not available to us at site of study. At present, the optical zoom magnifying endoscope is not widely used in clinical practice; however, recently the use of magnification has been increasing step by step all over the world. Future studies in NBI need to use optical high-end magnification scopes for characterization of lesions which may help contribute to better diagnostic accuracy. NBI studies also need to prove cost effectiveness when compared with conventional white light endoscopy in identifying pre-cancerous lesions. There is need to bring in adequate modifications in the current list of accessories used for NBI which can contribute to adequate specimen for the histopathologist to comment. We need long-term multicenter randomized studies to compare NBI studies with conventional white light endoscopy in routine surveillance colonoscopies and studying the long term outcomes (at least 10 years) which might contribute to substantial results.

Conclusion

To conclude, JNET classification was found to be very useful for predicting the histology of colorectal polyps (type-1, -2A, and -3 polyps). It did not correlate with HP findings in type-2B lesions in this study, which suggest that ability of type 2B to identify HGD or SM-s carcinoma is not significant. Owing to slightly lower sensitivity for type 2B, it needs additional investigation using pit pattern diagnosis. The JNET type-2B lesions encompass a variety of colorectal tumors and majority of these exhibit type-2A/2B borderline findings. In such cases, endoscopists should perform magnifying chromoendoscopy followed by a pit pattern diagnosis.

Conflict of Interest

None declared.

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