

Narrow-band imaging endoscopy is advantageous over conventional white light endoscopy for the diagnosis and treatment of children with Peutz-Jeghers syndrome

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Abstract

Using narrow-band imaging (NBI), the micro morphology of polyp surfaces was visualized at high resolution when the contrast between the lesions and the surrounding tissue areas was intensified. The objective of the study was to compare NBI and conventional white light endoscopy (C-WLI) for diagnostic efficacy and treatment of children with Peutz-Jeghers syndrome (PJS), a rare autosomal dominant-genetic disease.

We retrospectively analyzed the clinical data of 18 patients diagnosed with PJS and 72 diagnosed with juvenile polyps during the same time period. Endoscopy was used to observe the morphology of polyps, which were classified according to the Kudo pit pattern. Eighty-two and 76 polyps were resected using endoscopy from PJS and juvenile polyp patients, respectively, and pathologically examined for comparison with NBI or C-WLI endoscopic observations.

With NBI, 57 (69.5%) type I, 10 (12.2%) type II, and 13 (15.9%) type III polyps were identified in 82 (100%) polyps excised from 18 PJS patients, whereas 69 (88.5%) type I, 5 (6.4%) type II and 4 (5.1%) type III were identified in 78 (100%) of polyps removed from 72 juvenile polyp patients. The combined ratios of types II and III were higher in PJS (28.1%) than in juvenile polyp patients (11.5%). Pathological diagnosis identified 69 of 82 PJS polyps as hamartoma and 13 as adenoma, whereas NBI detected 10 adenomas and C-WLI only 4. The sensitivity, specificity, and accuracy of NBI in the diagnosis of adenoma were 76.9%, 97.1%, and 93.9%, respectively, whereas those of C-WLI were 30.8%, 94.2%, and 84.1%.

NBI endoscopy had higher sensitivity and specificity than C-WLI for the diagnosis of adenomatous polyps and is recommended for the diagnosis, characterization, and resection of polyps in children with PJS.

Abbreviations: C-WLI = conventional white light endoscopy, HE = hematoxylin and eosin, M-NBI = magnifying-NBI, NBI = narrow-band imaging, PJS = Peutz-Jeghers syndrome.

Keywords: children, diagnosis and treatment, NBI endoscopy, Peutz-Jeghers syndrome

1. Introduction

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant genetic disorder.^[1] Both sexes can carry the gene, and approximately 30% to 50% of patients have a family history of the disease.^[2] Gastrointestinal polyps found in PJS patients were often multiple hamartomas, with sizes varying from 1 to >5 cm.^[3] The clinical characteristics of PJS are skin or mucosa pigmentation, gastrointestinal polyps, and predisposition to benign and various malignant tumors such as adenocarcinoma.^[4] The incidence rate of hamartoma was reported to be 41.8% in

PJS patients, in which 51.5% of the cases were hamartoma with a size of 1 to 2 cm, and 13 patients who had both hamartoma and adenoma.^[5] Wang Zhenjun et al (2000) comprehensively analyzed 169 cases of PJS, and found that the incidence rate of malignant tumors was 20.1%, emphasizing the importance of accurate clinical diagnosis of this disease for early therapeutic intervention to prevent the development of cancer.^[6]

To diagnose and differentiate between typical hamartomatous polyps and adenoma or carcinoma, different types of endoscopy such as pigment endoscopy, magnifying endoscopy, ultrasonic endoscopy, and NBI endoscopy have been used.^[7] However, to differentiate between and categorize different types of polyp is difficult with morphological observation alone; endoscopic biopsies must be performed before implementing an appropriate therapeutic strategy. Suzuki et al (2015) reported a case of a patient with duodenal PJ-type hamartomatous polyps, in which they suggested that in the case of patients with these types of polyps, associated signs and symptoms should be evaluated as well, and that patients should undergo upper intestinal endoscopy, colonoscopy, as well as whole-body screening. They proposed that solitary PJ-type hamartomatous polyps should be distinguished as solitary or as an incomplete type of PJS, and these polyps should be treated by endoscopic or surgical resection.^[8] Some studies have shown that a minimally invasive endoscopic resection via enteroscopy of PJS polyps is safer and easier than laparotomy.^[9,10]

Editor: Abd Elrazek Abd Elrazek.

The authors report no conflicts of interest.

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Medicine (2017) 96:19(e6671)

Received: 17 October 2016 / Received in final form: 5 March 2017 / Accepted: 31 March 2017

<http://dx.doi.org/10.1097/MD.0000000000006671>

Recently, narrow-band imaging (NBI) has been introduced as a new method to examine polyps and diagnose PJS in children.^[11] Conventional white light endoscopy (C-WLI) often fails to diagnose PJS or misdiagnose early gastric mucosal carcinoma, especially micro concave gastric mucosal carcinoma. In contrast, magnifying-NBI (M-NBI) combined with WLI enables us to observe the gastric mucosal tissue structure and detailed vascular morphology, reducing the number of necessary biopsies required because of the highly accurate detection of the prominent mucosal structure. A multicenter prospective randomized controlled study in Japan has demonstrated that compared to C-WLI or M-NBI alone, M-NBI combined with C-WLI yielded a higher diagnostic accuracy, sensitivity, and specificity in patients with microconcave gastric mucosal carcinoma.^[12] However, a comparison of the diagnostic sensitivity, specificity, and accuracy between NBI and C-WLI endoscopy has not yet been made for PJS.

We retrospectively analyzed clinical data of 18 PJS patients treated in our hospital from June 2009 to August 2015. To compare between NBI and C-WLI for diagnostic accuracy, sensitivity, and specificity, we analyzed the number and size of polyps and the malignant transformation rate in these patients. We found that NBI endoscopy had a higher sensitivity and specificity than C-WLI endoscopy for the classification of PJS.

2. Materials and methods

2.1. Patients

In our hospital, 18 children were diagnosed with PJS and 72 simultaneously diagnosed with juvenile polyps from June 2009 to August 2015. The age of the patients ranged from 5 to 15 years, and the average was 7.6 years. We isolated 82 polyps and 76 polyps from PJS and juvenile polyp patients, respectively.

Patients' lesions were examined by C-WLI and NBI endoscopy and endoscopic images were recorded and analyzed. The polyps were endoscopically excised for pathological analysis to evaluate the diagnostic accuracy, sensitivity, and specificity of C-WLI and NBI endoscopy. This study was approved by the ethics committee of our hospital and family members of all patients signed consent forms for the endoscopic examination. The study was carried out according to the guidelines of our responsible governmental agency.

2.2. Endoscopy

The procedure for the NBI endoscopic examination was the same as for general colonoscopy. An endoscope mirror was inserted into the ileocecal junction in a white light mode and the whole colon was examined and observed by return of the reflected light. The micromorphology of the polyp surface (including pit patterns) was endoscopically observed. According to Kudo classification,^[13] the pit patterns were divided into 5 types: type I, round; type II, star or papillary; type III, tubular or disc; type IV, branching or gyriiform (Fig. 1A–C and E, respectively); and type V, irregular or nonstructured (image not shown).

2.3. Pathological examination

The excised polyps were fixed with formalin, dehydrated with gradient ethanol, and embedded in paraffin, followed by hematoxylin & eosin (HE) staining after being sectioned and mounted onto microscope slides (Fig. 1D). Patients' histopathological diagnosis was performed and patients were subjected to postoperative follow-up colonoscopy. Two experts with >10 years' experience in endoscopic operations completed all procedures including endoscopic diagnosis.

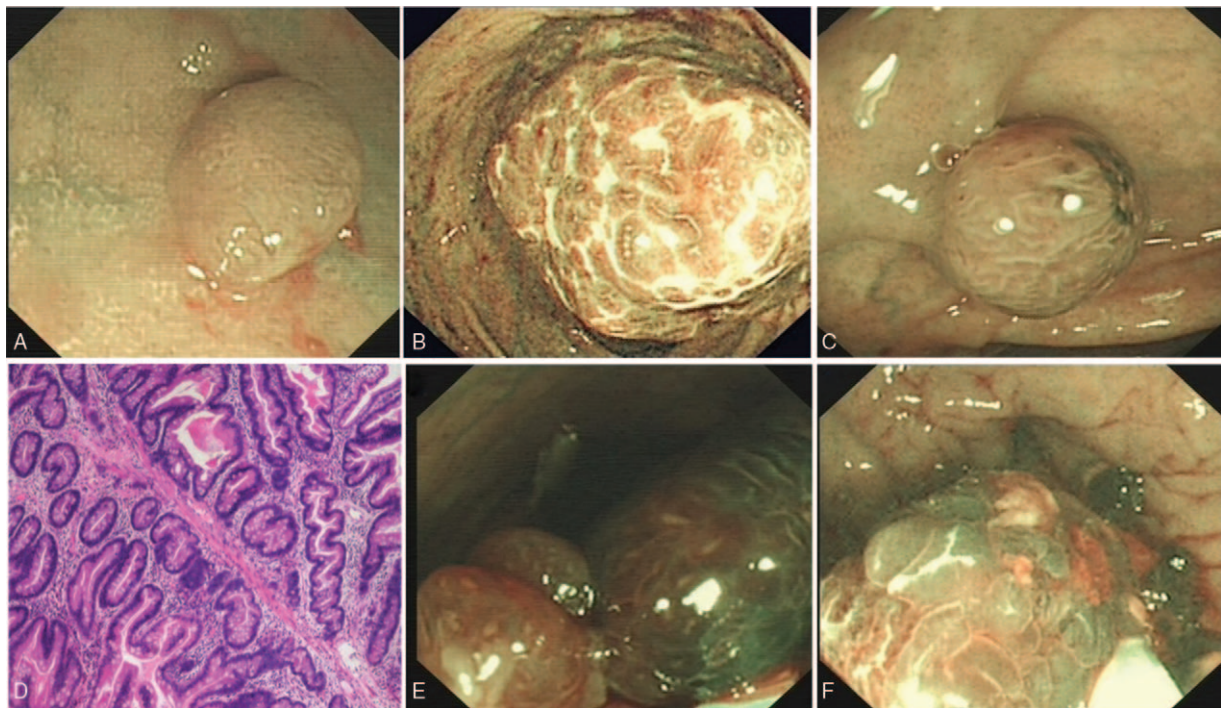


Figure 1. Images of pit patterns observed using narrow-band imaging. (A) Type I, dot-like pit pattern; (B) type II, star, papillary, or interleaving pit pattern; (C) type III, tubular or disc; (D) Peutz-Jeghers syndrome polyp pathology; (E) type IV, branching or gyriiform. (F) The polyp was changed to a purple color after polyp occlusion with titanium clips.

2.4. Endoscopic therapy for PJS patients

To resect PJS polyps with a diameter of <2cm, we employed a high-frequency electric excision method in which electrical heat dries the tissue surface and denatures protein to coagulation causing necrosis. For larger polyps with a diameter of >2cm, we used metal clips to block the blood supply and ligate the polyps, and then performed the excision. The following equipments were used: Olympus GIF-XQ240/260 gastroscopy (Olympus, Tokyo, Japan); Olympus PCF-Q260AI colonoscopy (Olympus, Tokyo, Japan); ERBE VIO 200S high frequency electric generator (ERBE, Marietta, GA); OLYMPUS SD-9U1 trap; and Olympus metal titanium clips for endoscopic resection (Olympus, Tokyo, Japan). We used Olympus CV-260SL pediatric digestive endoscopy with NBI function (Olympus, Tokyo, Japan) (Fig. 1F).

2.5. Statistical analysis

Statistical analysis was performed with SPSS Statistics for Windows (Version 22.0; IBM Corp, Armonk, NY). Normally distributed measurement data were analyzed by a *t* test and enumeration data by a χ^2 test, and the accuracy, sensitivity, and specificity of NBI and C-WLI endoscopies determined. $P < .05$ was considered to be statistically significant.

3. Results

3.1. General information about the patients

A total of 82 polyps and 76 polyps were identified in 18 PJS and 72 juvenile polyp patients, respectively. In PJS patients, 66.7% of polyps were in the colon and 22.2% in the stomach, whereas in juvenile polyp patients, 97.2% of polyps were in the colon. Pathological diagnosis demonstrated that 84.1% and 15.9% of PJS polyps were hamartomas and adenomas, respectively, whereas 96.2% of juvenile polyps were hamartomas, with adenomas accounting for only 1.3% of polyps.

3.2. Comparison of the morphological characteristics of PJS and juvenile polyps with NBI endoscopy

According to Kudo pit patterns, we classified polyps with MBI endoscopy and found that type I accounted for 69.5% and 88.5% in PJS and juvenile polyps, respectively (Table 1). Type II

Table 1
General information on patients with PJS and juvenile polyps.

	82 PJS polyps (18 patients)	78 Juvenile polyps (72 patients)	P
Age, y (mean \pm SD)	7.6 \pm 2.3	8.2 \pm 3.5	.492
Sex			
Male	10 (55.6)	40 (55.6)	1.000
Female	8 (44.4)	32 (44.4)	1.000
Average polyp size, cm	0.74 \pm 1.36	0.86 \pm 1.28	.564
Skin pigmentation	4 (22.2)	0 (0.0)	.002
Polyp location			
Colon	12 (66.7)	70 (97.2)	.354
Stomach	4 (22.2)	1 (1.4)	.002
Others	2 (11.1)	1 (1.4)	.053
Pathological diagnosis			
Adenoma	13 (15.9)	1 (1.3)	.003
Hamartoma	69 (84.1)	75 (96.2)	.562

PJS = Peutz-Jeghers syndrome, SD = standard deviation.

accounted for 12.2% and 6.4% and type III for 15.9% and 5.1% in PJS and juvenile polyps, respectively. The combined ratio of type II and III in PJS polyps (28.1%) was significantly higher than in juvenile polyps (11.5%), indicating that a greater number of PJS polyps were at an advanced stage.

3.3. Comparison of the sensitivity, specificity, and accuracy between NBI and C-WLI endoscopy in the diagnosis of PJS polyps

Pathological examination identified 13 adenomatous polyps in 82 PJS polyps excised from 18 patients, whereas NBI endoscopy detected 10 adenomatous polyps, and C-WLI only 4 polyps (Table 2). We retrospectively analyzed clinical data of the 18 PJS patients regarding the number and size of polyps and the malignant transformation rate, to assess the diagnostic efficacy of NBI and C-WLI. The sensitivity, specificity, and accuracy of NBI endoscopy in the diagnosis of adenomatous polyps were 76.9%, 97.1%, and 93.9%, respectively, whereas those of C-WLI were 30.8%, 94.2%, and 84.1% (Table 3). Thus, the diagnostic sensitivity of NBI was significantly greater than that of C-WLI ($P < .05$), showing the superiority of NBI over C-WLI in the detection of adenomatous polyps. However, in diagnostic accuracy and specificity, no significant statistical difference was observed between these 2 methods. Additionally, NBI and C-WLI demonstrated similar sensitivity to the diagnosis of hamartoma (Table 4).

3.4. Endoscopic therapy

Patients diagnosed with PJS were subjected to NBI endoscopic therapy. In a high-frequency electric excision of 82 polyps from these patients, metal titanium clips were used for 14 larger polyps to block the blood supply and ligate polyps. After clipping, a gradual color change from purple to black was observed under NBI endoscopy (Fig. 1F). Flat polyps, which are often premalignant and difficult to detect, were subjected to endoscopic mucosal resection. A clearer display of the lesion by NBI endoscopy enabled us to achieve more thorough treatment.^[14,15]

4. Discussion

NBI endoscopic observations revealed that PJS polyps classified in Kudo pit pattern types II or III accounted for 28.1%, a value that was significantly higher than juvenile polyps, which accounted for only 11.5%. In addition, 2 lesions of PJS polyps were type IV, considered to be a neoplastic change. A comparison of the diagnostic efficacy between NBI and C-WLI for PJS adenomatous polyps demonstrated that the sensitivity, specificity and accuracy of NBI were 76.9%, 97.1%, and 93.9%,

Table 2
Comparison of the morphological classification of PJS polyps and juvenile polyps with NBI endoscopy.

Class type	Number of lesions	Juvenile polyps	PJS polyps
Type I	126	69 (88.5%)	57 (69.5%)
Type II	15	5 (6.4%)	10 (12.2%)
Type III	17	4 (5.1%)	13 (15.9%)
Type IV	2	0	2 (2.4%)
Type V	0	0	0
Total	160	78 (100%)	82 (100%)

NBI = narrow-band imaging, PJS = Peutz-Jeghers syndrome.

Table 3

Comparison of diagnostic efficacy of C-WLI and NBI endoscopy in the identification of PJS adenomatous polyps.

Groups	Methods	Accuracy	Sensitivity	Specificity
NBI group	NBI	93.9%	76.9%	97.1%
White light group	C-WLI	84.1%	30.8%	94.2%
<i>P</i>		.630	.001	.864

P < .05 is considered to be statistically significant. C-WLI = conventional white light endoscopy, NBI = narrow-band imaging, PJS = Peutz-Jeghers syndrome.

respectively, and those of C-WLI were 30.8%, 94.2%, and 84.1%, suggesting that the efficacy of NBI was generally greater than that of C-WLI, in agreement with the findings of other studies.^[16–18] Although a statistically significant difference was found only in sensitivity (*P* < .05), it is anticipated that the higher sensitivity of NBI will enable surgeons to distinguish ambiguous micromorphology and help their prediction and judgment of the pathological properties of PJS polyps. Thus, employment of NBI greatly improves the sensitivity and specificity of endoscopic diagnosis.^[16]

In treating PJS patients with C-WLI endoscopy, we found that it was difficult to detect polyps with a diameter of <5 mm, as well as some of the wide-based polyps that often have a tendency to malignant transformation.^[19] In contrast, NBI endoscopy could display the mucosal vascular network and increase the contrast between lesions and the surrounding tissues, greatly improving the detection and diagnosis of flat-type lesions.

During endoscopic treatment, we used titanium clips to block the blood supply to polyps with a diameter >2 cm or wide-based polyps with a diameter >1 cm. A color change of the polyp after clipping was more distinctly visualized with NBI than C-WLI endoscopy. NBI endoscopy filters white light into 3 narrow bands of blue, green, and red light by special optical filters with 485 to 515 nm, 430 to 469 nm, and 400 to 430 nm wavelengths, respectively, enhancing the intensity of each wavelength. Because of its short wavelength (415 nm), blue light penetrates only into a shallow layer of the mucosa, and its wavelength overlaps with the light absorption peak of hemoglobin, which makes NBI endoscopy propitious in examining pit patterns and superficial vessels of the digestive tract mucosa. Green light has strong tissue penetrating abilities and is suitable for submucosal blood vessel display, whereas red light penetrates relatively deeper and enables the visualization of clusters of large blood vessels in the mucosal deep layer. The images obtained with these 3 intensified light bands were shown on the monitoring device through an image loop integration of the endoscopic system, and the structural details of different mucosal layers could be examined on a display monitor. NBI endoscopic examination is minimally invasive, and visualization can be carried out easily by switching 2 kinds of light sources on the instrument.

Table 4

Comparison of the diagnostic specificity between pathology C-WLI and NBI endoscopies in PJS polyps.

	Pathological diagnosis	C-WLI endoscopy	NBI endoscopy	<i>P</i>
Adenoma	13 (100%)	4 (30.8%)	10 (76.9%)	.0009
Hamartoma	69 (100%)	61 (88.4%)	63 (91.3%)	.8963

Comparison of NBI endoscopy and traditional white light endoscopy; *P* < .05. C-WLI = conventional white light endoscopy, NBI = narrow-band imaging, PJS = Peutz-Jeghers syndrome.

Flexible spectral imaging color enhancement (FICE) and NBI are digital chromoendoscopy methods that enhance endoscopic images without the necessity of a dye. Apart from their safeness for polyp detection, digital chromoendoscopy also enables the endoscopist to select a concurrent intervention like endomucosal resection, submucosal dissection, or polypectomy by enabling endoscopic histological diagnosis. The importance of FICE and NBI optical systems results from their ability to detect polyp histology, as endoscopic histological diagnosis predictions decrease costs by preventing unnecessary polypectomies and screening endoscopies. Furthermore, digital chromoendoscopy may decrease the development of cancer by increasing the detection and removal rates of neoplastic diminutive polyps and flat adenomas. Unfortunately, at present, FICE is not used to treat pediatric disease.

In conclusion, NBI endoscopy enables the visualization of the micromorphology of polyp surface (pit patterns) at high resolution and intensifies the contrast between the lesions and the surrounding tissue.^[20] This results in a higher sensitivity and specificity for the diagnosis of adenomatous polyps compared to C-WLI endoscopy. In addition, NBI endoscopy is minimally invasive and simple to operate. Hence, NBI is a preferred method to diagnose and characterize, as well as to remove, digestive tract polyps in children with PJS. However, the number of cases examined in our study was relatively small and because of a recent introduction of NBI to children's treatment in China, there are many shortcomings that remained to be further studied.

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