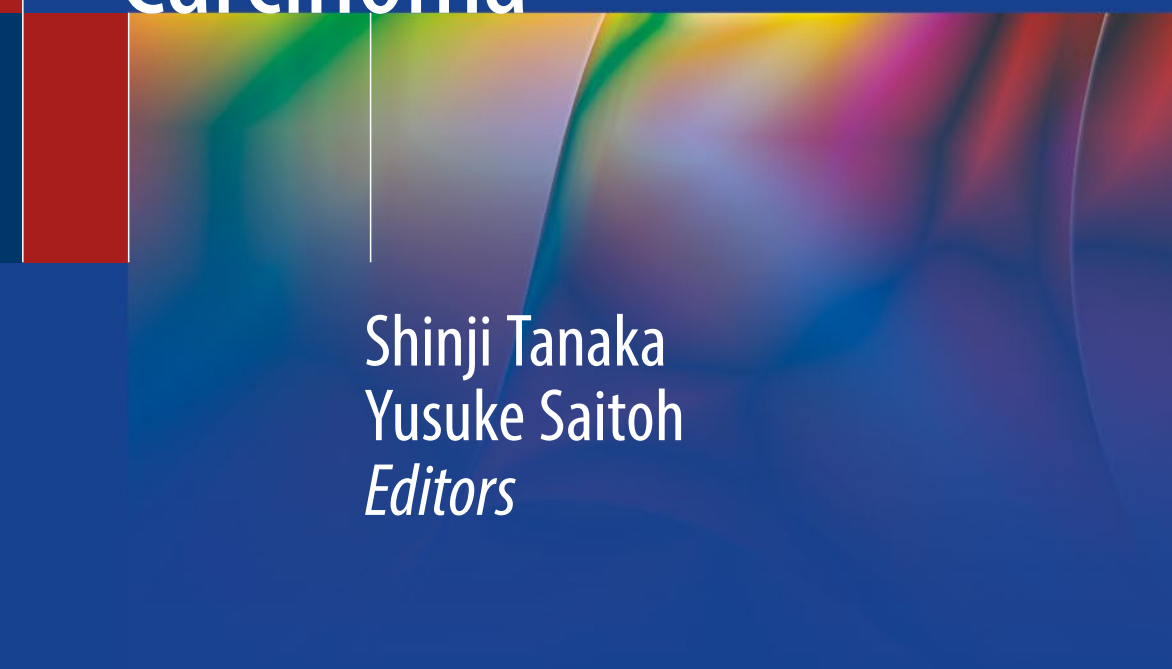
Endoscopic Management of Colorectal T1(SM) Carcinoma



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Preface

At present, many T1 (SM) colorectal carcinomas have been diagnosed and treated by endoscopy or surgery. Also, it has been clarified that even for T1b (SM deep invasive) cancer, if there are no other lymph node metastatic risk factors such as unfavorable histologic components, vessel involvement, and a high budding grade, the estimated lymph node metastatic risk is 1.2–1.4%. On the other hand, recent progress in endoscopy such as endoscopic submucosal dissection (ESD) has made it possible to resect Tis/T1 colorectal cancer endoscopically en bloc regardless of its size. Endoscopic treatment is gradually becoming more commonly used to achieve excisional biopsy even for cT1b colorectal carcinoma like this.

Nevertheless, in order to generalize this practice, we must solve several issues. First, precise invasion depth diagnosis prior to endoscopic resection of the lesion in order to achieve complete en bloc resection is important. En bloc resection is essential to determine the precise histologic diagnosis for deciding curability. Second, generalization of the endoscopic resection technique (polypectomy, endoscopic mucosal resection (EMR), ESD) for en bloc resection is important. Third, adequate handling of the endoscopically resected specimen and precise histologic diagnosis are essential to determine curability. For endoscopic treatment of T1 (SM) colorectal carcinoma, generalization and quality control of these three points are not only important but essential.

Accordingly, the publication of this educational text has been planned to address the above-mentioned issues. We hope that this book will assist in daily clinical practice for treatment of T1 (SM) colorectal carcinoma.

Hiroshima, Japan — Shinji Tanaka
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July 2019

Contents

Part I
The Endoscopic Diagnosis of Colorectal T1(SM) Carcinoma

Chapter 1
Conventional Colonoscopy Including Indigo Carmine Dye Spray

Yusuke Saitoh and Mikihiro Fujiya

Abstract With recent advances in endoscopic diagnostic and therapeutic technology, the preoperative endoscopic diagnosis of T1 (submucosal) carcinomas will become more important for determining whether detected T1 carcinoma can be cured by endoscopy alone (lesions with <1000 μm submucosal invasion) or should be treated by surgery (lesions with ≥1000 μm submucosal invasion). Useful conventional colonoscopic findings suggestive of polypoid-type T1b carcinomas are as follows: an expansion appearance, tumor stiffness or unevenness in the comprehensive view, coarse surface findings, converging folds toward the tumor, poor extension of the surrounding colonic wall, and stiffness or deformity of the colonic lumen. Similarly, useful conventional colonoscopic findings suggestive of flat and depressed-type T1b carcinomas are as follows: an expansion appearance, tumor stiffness or unevenness, protrusion in the depression surface, uneven depression surface, strong redness, converging folds toward the tumor, colonic wall deformity, stiffness of the colonic lumen, and table-like protrusion. If at least one of these colonoscopic findings is detected, then surgery should be considered. However, if none of these colonoscopic findings are detected, endoscopic resection (i.e., endoscopic polypectomy, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD) depending on the lesion's shape and size) can be performed.

Keywords Colorectal T1 (SM) carcinoma · Conventional colonoscopy · Indigo carmine dye spray · Invasion depth diagnosis · Endoscopic mucosal resection · Endoscopic submucosal dissection

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1.1 Introduction

In recent years, the number of colorectal carcinoma cases has increased in Japan, and colorectal cancer was the third most common cause of cancer-related death in men and the most common cause in women from 2003 [1]. The early detection of colorectal carcinomas is expected to become an increasingly important issue for reducing the rate of colorectal cancer death, as the prognosis of early colorectal carcinomas is satisfactory, with a 5-year survival rate exceeding 90%, and a complete cure can be obtained by endoscopic resection and/or radical surgery [2].

Recent advances in the endoscopic diagnosis and treatment of colorectal carcinomas have been remarkable, with the increased detection of flat and depressed (F&D) tumors [3] and the use of magnifying endoscopy with narrow-band imaging (NBI) [4] and high-frequency ultrasound probes (HFUPs) [5] in the diagnostic aspect and the increasing use of endoscopic mucosal resection (EMR) [6] and endoscopic submucosal dissection (ESD) [7] for large F&D tumors in the therapeutic aspect.

Endoscopic treatment for early colorectal carcinomas allows for less invasive treatment, resulting in a good quality of life (QOL) for patients. However, this approach is indicated for lesions with little risk of lymph node metastasis, with surgery recommended as a radical treatment for T1 carcinomas on principle as approximately 10% of all T1 carcinomas have lymph node metastases [8].

The increase in the aging population is expected to result in an increase in the number of patients requiring follow-up after endoscope resection without additional surgery due to systemic complications, even if the resected lesion carried some risks of lymph node metastasis. A preoperative endoscopic diagnosis will therefore prove important for determining whether a detected lesion can be cured by endoscopy alone or if it should be considered to treat by radical surgery.

1.2 Indication of Endoscopic Resection for Colorectal Carcinomas

Endoscopic resection is basically indicated for colorectal lesions with little risk of lymph node metastasis, such as benign adenomas, intramucosal carcinomas (Tis) (corresponding to severe dysplasia in Western countries), and focally extended T1 (T1a) carcinomas.

According to the 2014 guidelines of the Japanese Society for Cancer of the Colon and Rectum (JSCCR) for the treatment of colorectal cancer [8], T1 carcinomas histologically diagnosed with a negative vertical margin and favorable histologic grade (papillary adenocarcinoma or tubular adenocarcinoma) with a submucosal invasion depth of <1000 μm, no vascular permeation, and grade 1 tumor budding (low grade) can be followed up without additional surgery after endoscopic resection. By referencing the abovementioned histopathological findings, we can reduce the rate of unnecessary additional surgery.

However, the only one of these histopathological findings that can be assessed before endoscopic resection is the invasion depth. Therefore, determining preoperatively whether a detected lesion is a T1a carcinoma (submucosal invasion depth <1000 μm) or T1b carcinoma (submucosal invasion depth ≥1000 μm) is of great importance with regard to the choice of therapy (endoscopic resection vs. surgery).

1.3 Conventional Colonoscopic Findings for Determining the Choice of Therapy (Submucosal Invasion Depth <1000 or ≥1000 μm)

It is important to discriminate between T1 carcinoma with a submucosal invasion depth of <1000 μm (T1a) that may be completely cured by endoscopic resection alone and that with a submucosal invasion depth of ≥1000 μm (T1b) that should be considered to treat with surgery.

From a prospectively analysis [9], conventional colonoscopic findings including 0.1% indigo carmine dye spray without magnifying colonoscopy or HFUPs, which are useful for choosing the therapy, were described in each macroscopic type.

1.3.1 Conventional Colonoscopic Findings Suggestive of Polypoid-Type T1b Carcinoma

Useful conventional colonoscopic findings suggestive of polypoid-type T1b carcinomas are shown in Table 1.1. An expansion appearance (protrusion and overextension of the tumor and/or surrounding normal mucosa, like a submucosal tumor), tumor stiffness or unevenness in the comprehensive view, coarse surface findings (surface roughness) in the surface property, converging folds toward the tumor (two

Table 1.1 Conventional colonoscopic findings suggestive of polypoid type T1b (≥1000 μm) carcinoma lesions

Univariate analyses with Mann-Whitney U			
Colonoscopic findings	*p* Value	Colonoscopic findings	*p* Value
Comprehensive view		**Property of the tumor surroundings**	
Expansion appearance	0.0369	Converging folds towards the tumor	0.0111
Tumor stiffness	0.0001	Deformity of the colonic lumen	0.0004
Tumor unevenness	0.0192	Poor extension of the surrounding colonic wall	0.0028
Surface property			
Coarse surface findings (surface roughness)	0.0235		

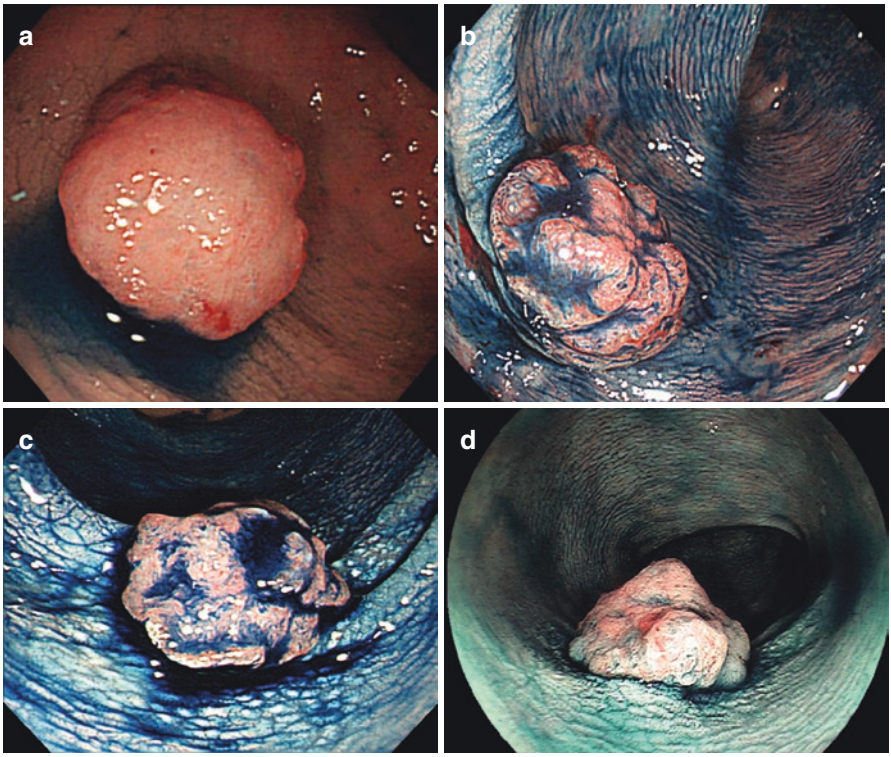

Fig. 1.1 Suggestive colonoscopic findings for polypoid-type T1b (≥1000 μm) carcinomas: (**a**) expansion appearance, (**b**) tumor stiffness, surface unevenness, (**c**, **d**) converging folds toward the tumor and stiffness of the colonic lumen

or more mucosal folds converging toward the tumor), poor extension of the surrounding colonic wall, and stiffness or deformity of the colonic lumen among properties of the tumor surroundings were observed with significantly high frequency in polypoid-type T1b carcinomas. Representative objective conventional colonoscopic findings are shown in Fig. 1.1.

1.3.2 Conventional Colonoscopic Findings Suggestive of F&D-Type T1b Carcinoma

Similarly, useful conventional colonoscopic findings suggestive of F&D-type T1b carcinomas are shown in Table 1.2. An expansion appearance, tumor stiffness or unevenness in the comprehensive view, protrusion in the depression surface, uneven depression surface, strong redness in the surface property, converging folds toward the tumor, colonic wall deformity, stiffness of the colonic lumen, table-like

Table 1.2 Conventional colonoscopic findings suggestive of F&D type T1b (≥1000 μm) carcinoma lesions

Univariate analyses with Mann-Whitney U			
Colonoscopic findings	*p* Value	Colonoscopic findings	*p* Value
Comprehensive view		**Property of the tumor surroundings**	
Expansion appearance	<0.0001	Converging folds toward the tumor	0.0087
Tumor stiffness	<0.0001	Deformity of the colonic lumen	0.0052
Tumor unevenness	0.0458	Poor extension of the surrounding colonic wall	0.0331
Surface property		Table-like protrusion	0.0037
Protrusion in the depression surface	0.0063	**Technical aspects**	
Uneven depression surface	0.0409	No findings of air deformity	0.0003
Coarseness	<0.0001	Easy bleeding	0.0381
Strong redness	<0.0001		

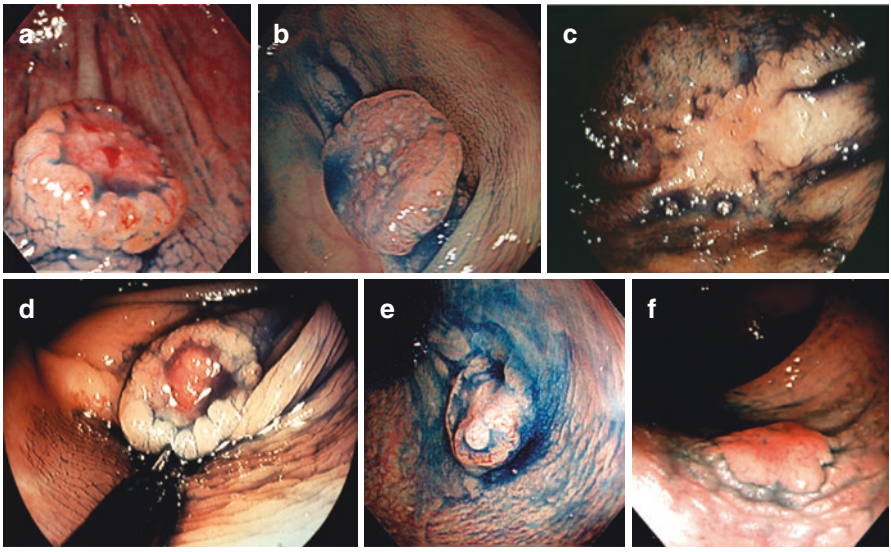

Fig. 1.2 Suggestive colonoscopic findings for "flat- and depressed-type" T1b (≥1000 μm) carcinomas (part 1): (**a**) expansion appearance, (**b**) tumor stiffness, (**c**) converging folds toward the tumor, (**d**, **e**) deep and/or uneven depression surface, (**f**) strong redness

protrusion in the property of the tumor surroundings, and negative air deformity (tumor deformity not seen as air decreasing by the aggregated submucosal cancer mass) were observed with significantly high frequency in F&D-type T1b carcinomas. Representative objective conventional colonoscopic findings are shown in Figs. 1.2 and 1.3.

When a lesion is detected, the application of indigo carmine dye spray should be performed. If at least one of these colonoscopic findings is detected, then surgery

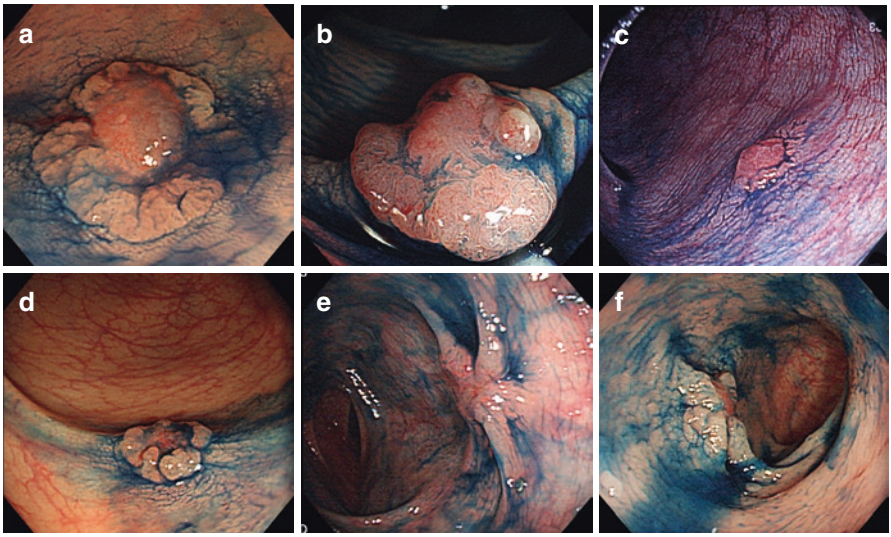

Fig. 1.3 Suggestive colonoscopic findings for "flat- and depressed-type" T1b (≥1000 μm) carcinomas (part 2): (**a**, **b**) protrusion in the depression surface, (**c**) wall deformity, (**d**–**f**) wall deformity and converging folds toward the tumor, (**e**, **f**) table-like elevation

should be considered. However, if none of these colonoscopic findings are detected, endoscopic resection (i.e., endoscopic polypectomy, EMR, and ESD depending on the lesion's shape and size) can be performed.

1.3.3 Problems Diagnosing the Invasion Depth with Conventional Colonoscopy

The colonoscopic findings mentioned above are important for determining the colonoscopic invasion depth preoperatively, but the accuracy rate of the invasion depth diagnosis is not satisfactory, being around 75% even at expert institutions in Japan [9]. We sometimes encounter cases in which determining the preoperative invasion depth via conventional colonoscopy alone is difficult. Therefore, in such cases, the combination use of NBI and magnifying colonoscopy, along with the additional use of HFUPs or X-ray (barium enema study [10]), should be considered.

1.4 Conclusion

Objective conventional colonoscopic findings for each macroscopic type were described. When a lesion suspected of being T1 carcinoma is detected, we should pay close attention to the colonoscopic findings mentioned above. These conventional colonoscopic findings are objective and will prove useful for determining the most suitable therapy, especially in T1 carcinomas.

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Chapter 2
Magnifying Endoscopy: Pit Pattern Diagnosis

Hiro-o Yamano

Abstract Endoscopic diagnosis is the most important part of endoscopy. Recently, we diagnosed the so-called "pit pattern diagnosis" using magnifying endoscopy, which makes it possible to perform high-level diagnosis that approximates pathological diagnosis. In pit pattern classification (Kudo's classification), the proper rate of discrimination was reported to be approximately 96–98% between tumors and non-tumors and 70–90% between adenoma and cancer. In submucosal invading cancer, the risk of vascular infiltration and lymph node metastasis is proportional to the vertical invading (T1) of the cancer. Therefore, it is necessary to diagnose the degree of invading into the submucosa before endoscopic treatment of early colorectal cancer. Magnifying endoscopy showed that when used as an indicator of deep submucosal invading of the type VN, an appropriate discrimination rate is about 90%. Thus, a qualitative diagnosis with high accuracy can be achieved with magnifying endoscopy.

Keywords Endoscopic diagnosis · Magnifying endoscopy · Pit pattern diagnosis Kudo's classification · Colorectal tumor · Colorectal neoplasm · Colorectal cancer

2.1 Introduction

Endoscopic diagnosis is the most important part of endoscopic examination because it will help us to decide the correct endoscopic treatment.

Several decades ago, although it was able to predict characteristics of the lesion, for example, macroscopic shape, depression, converged fold, size, etc., its accuracy was very low. The experience value and judgment of the individual endoscopist also had a great effect.

As a result, magnifying endoscopes were introduced in the early 1990s with the aim of high-quality diagnosis and standardization. The "pit pattern diagnosis" was

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established by using it, and we became able to predict pathological diagnosis as accurately as possible. In this chapter we will discuss the "pit pattern diagnosis."

2.2 Pit Pattern Classification: Kudo's Classification

Magnifying endoscopic diagnosis is based on observational studies of the surface microstructure for colorectal tumor by stereomicroscope performed on fixed resection specimens [1, 2]. A magnifying endoscope was developed with the aim of applying the findings obtained in these studies in vivo.

Kudo et al. called the surface microstructure "pit pattern", and they came to find a constant rule since "pit pattern" was analyzed corresponding to the pathological features and diagnosis. They established the magnifying endoscope diagnosis, that is, the "pit pattern diagnosis" or "Kudo's classification" [3]. The pit pattern can be observed by using two dyes, 0.2% indigo carmine and 0.04% crystal violet, in magnifying chromoendoscopy.

Currently, pit pattern is divided into six categories, from type I to type VN, and type VI is divided into two subclasses. The details are described below.

- Type I: This pattern consists of roundish pits as normal crypts, each 0.07 ± 0.02 mm in size (Fig. 2.1).
- Type II: This pattern comprises relatively large pits (0.09 ± 0.02 mm) with a star-like or onion-skin-like structure. This is the basic pit pattern of hyperplastic lesions. Recently, it has been reported that "type II open", whose crypt opened with this pit pattern, is a characteristic finding of SSA/P [4] (Fig. 2.2).
- Type IIIs: This pattern consists of tubular or roundish pits smaller than normal ones (0.03 ± 0.01 mm). We can see it in a depressed area of the lesion or depressed type of tumor (Fig. 2.3).

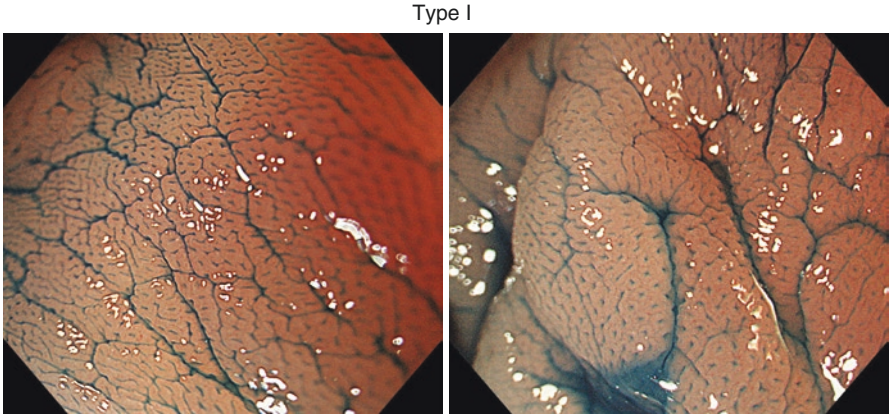

Fig. 2.1 Magnified image of normal mucosa in colon. We can recognize roundish pits as normal crypts

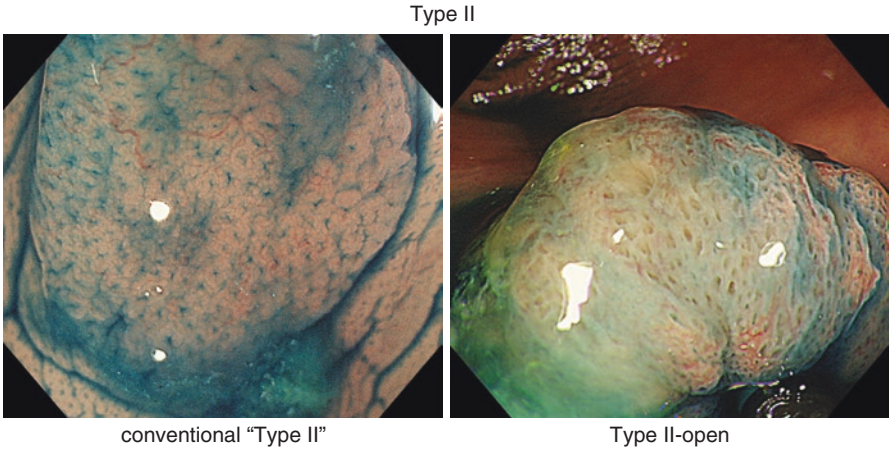

Fig. 2.2 Typical type II pit pattern consists of star-like or onion-skin-like surface structure (left). Type II-open pit pattern whose crypt opened with mucin producing is a characteristic finding of SSA/P (right)

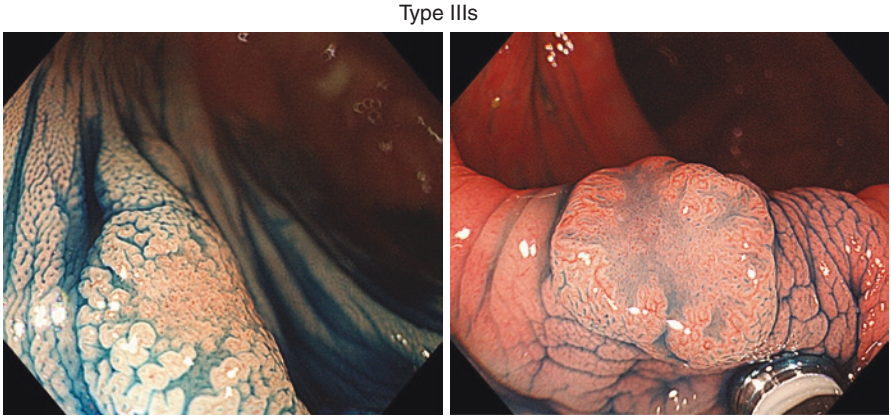

Fig. 2.3 Type IIIs pit pattern consists of tiny tubular or roundish pits, which are smaller than normal crypts of around mucosa

- Type IIIL: This pattern consists of tubular pits larger than normal ones (0.22 ± 0.09 mm). It is the basic pit pattern as a protruded and flat type of tubular adenoma (Fig. 2.4).
- Type IV: This refers to a sulcus-, branch- or gyrus-like pit pattern, such as tubulevillous and villous adenoma, although the gyrus-like pit pattern actually consists of an assembly of segmented grooves rather than pits; for convenience, it is included in this category (Fig. 2.5).
- Type VI: This pattern is similar to type IIIL, IIIs, and IV, but consists of disorder of the array, a size disparity, asymmetry, etc. Currently, it is divided into two subclasses, low grade and high grade irregularity. The former is high grade adenoma and intramucosal cancer, the latter is intramucosal cancer and slightly invading cancer (Fig. 2.6).

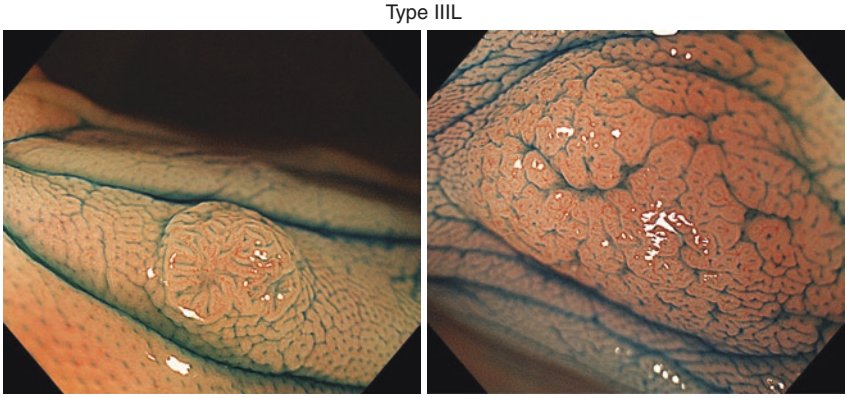

Fig. 2.4 Type IIIL pit pattern is composed of long tubular crypts (left). These are sometimes mixed with normal crypts in the inner area (right)

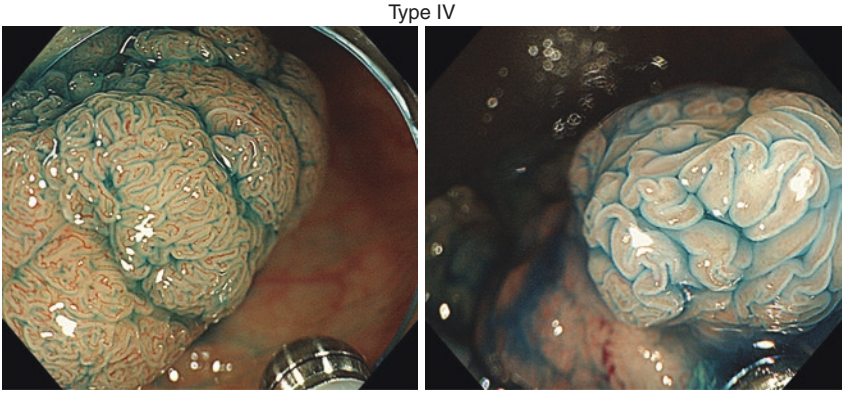

Fig. 2.5 Type IV pit pattern refers to a sulcus-, branch-, or gyrus-like surface structure

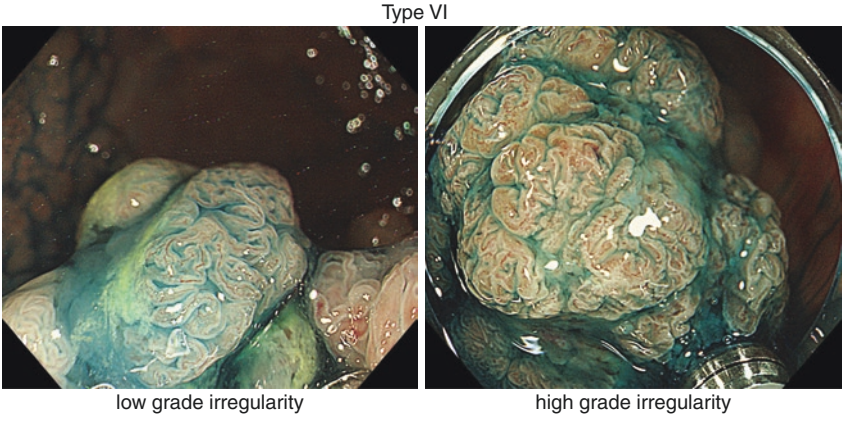

Fig. 2.6 Type VI pit pattern is similar to type IIIL, IIIS, and IV, but consists of disorder of the array, a size disparity, and asymmetry. The one with less of these irregularities is considered "low grade" (left), and the one with more irregularities is considered "high grade" (right)

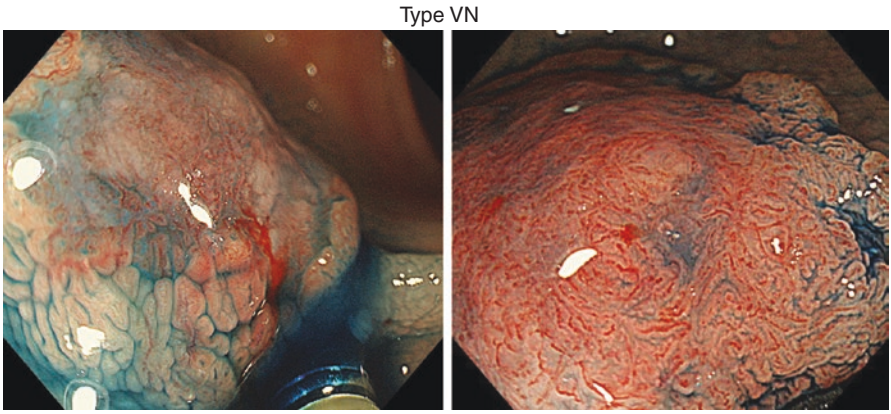

Fig. 2.7 Type VN pit pattern refers to lost (left) or broken down (right) surface structure

- Type VN: The surface structure disappears in this pattern and shows what became a so-called no structure. We can see it in a massive invading or advanced cancer type of tumor (Fig. 2.7).

2.3 Qualitative Diagnosis and Invading Depth Diagnosis

We can diagnose a lesion using magnifying endoscopy based on pit pattern classification in vivo without performing a biopsy of the lesion. The proper rate of discrimination was reported to be approximately 96–98% between tumors and non-tumors and 70–90% between adenoma and cancer. Thus, a qualitative diagnosis with high accuracy can be achieved with magnifying endoscopic observation [5–10].

It is necessary to diagnose the degree of submucosal invasion before performing endoscopic treatment in early colorectal cancer. The risks of vascular infiltration and lymph node metastasis are proportional to the vertical depth of submucosal invading cancer (T1). Moreover, to perform accurate pathological evaluation of endoscopically resected specimens, it is important to indicate the location of submucosal invading. Therefore, in the case of deep T1 cancer, endoscopic treatment is more likely to result in incomplete excision, and surgical treatment must be performed after endoscopic treatment [11].

The proper rate of discrimination of submucosal massive invading was reported to be approximately 70–80% by non-magnifying endoscopy [12, 13].

On the other hand, pit pattern diagnosis using magnifying endoscopy showed that the proper rate of discrimination was about 90% when the VN type was used as an indicator. However, the rate of protruded type lesions tends to be slightly lower than that of flat type lesions. Since diagnostic accuracy differs according to the macroscopic type and growth type of the lesion, appropriate diagnostic methods (IEE, EUS, etc.) should be combined as the situation requires [14–16].

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