

Preoperative endoscopic diagnosis of superficial non-ampullary duodenal epithelial tumors, including magnifying endoscopy

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Abstract

Superficial non-ampullary duodenal epithelial tumor (SNADET) is defined as a sporadic tumor that is confined to the mucosa or submucosa that does not arise from Vater's papilla, and it includes adenoma and adenocarcinoma. Recent developments in endoscopic technology, such as high-resolution endoscopy and image-enhanced endoscopy, may increase the chances of detecting SNADET lesions. However, because SNADET is rare, little is known about its preoperative endoscopic diagnosis. The use of endoscopic resection for SNADET, which has no risk of metastasis, is increasing, but the incidence of complications, such as perforation, is significantly higher than in any other part of the digestive tract. A preoperative diagnosis is required to distinguish between lesions that should be followed up and those that require treatment. Retrospective studies have revealed certain endoscopic findings that suggest malignancy. In recent years, several new imaging modalities have been developed and explored for real-time diagnosis of these lesion types. Establishing an endoscopic diagnostic tool to differentiate between adenoma and adenocarcinoma in SNADET lesions is required to select the most appropriate treatment. This review describes the current state of knowledge about preoperative endoscopic diagnosis of SNADETs, such as duodenal adenoma and duodenal adenocarcinoma. Newer endoscopic techniques, including magnifying endoscopy, may help to guide these diagnostics, but their additional advantages remain unclear, and further studies are required to clarify these issues.

Key words: Endoscopy; Duodenoscopy; Duodenal neoplasms; Narrow band imaging; Pathology

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Core tip: Because superficial non-ampullary duodenal epithelial tumor is rare, a preoperative endoscopic diagnostic technique to differentiate between adenoma and adenocarcinoma has not yet been established. Recently, many new imaging modalities have been developed and explored for use in the real-time diagnosis of these types of lesions. Newer endoscopic techniques, including magnifying endoscopy, may help to guide these diagnostics, but their additional advantages remain unclear, and further studies are required to clarify these issues.

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INTRODUCTION

Epithelial tumors of the duodenum are relatively rare^[1], with primary duodenal carcinomas comprising only approximately 0.5% of malignant gastrointestinal tumors^[2]. Duodenal adenomas are uncommon lesions with a reported prevalence of less than 0.4% in patients undergoing esophago-gastro-duodenoscopy^[3,4]. Surgical treatment of non-ampullary duodenal tumors can be invasive because of anatomical complexities. Recent developments in endoscopic technology, such as high-resolution endoscopy and image-enhanced endoscopy, may increase the chances of detecting superficial non-ampullary duodenal epithelial tumor (SNADET) lesions and allow their resection without surgery^[5,6]. The prognosis of patients with advanced duodenal carcinomas is poor^[7], and early detection and treatment are essential.

Endoscopic resection (ER) is a minimally invasive, local treatment that can be used in cases of SNADET with no risk of metastasis^[8]. However, the incidence of complications, such as perforation, that are associated with the use of ER to treat SNADET is significantly higher than in any other part of the digestive tract^[6,9,10] because of the thinness of the duodenal wall and its exposure to bile and pancreatic juice^[9,11,12]. A preoperative diagnosis is required to distinguish between lesions that should be followed up and those that require treatment. Follow-up without ER for low-grade adenoma (LGA) is acceptable because its risk of progression to cancer is approximately 5%^[9,13]. However, because SNADET is rare, much remains unknown about its preoperative endoscopic diagnosis.

SNADET is defined as a sporadic tumor that is confined to the mucosa or submucosa that does not arise from Vater's papilla, and it includes adenoma and

adenocarcinoma. This review focuses on the present status of the preoperative endoscopic diagnosis of SNADETs.

HISTOPATHOLOGICAL DIAGNOSES REFERRED TO THE REVISED VIENNA CLASSIFICATION AND CLINICAL MANAGEMENT

Recently, a new set of categories for classifying gastrointestinal neoplasias (*i.e.*, the Vienna classification) has been proposed (Table 1) to bridge the East-West gap^[14]. Adenomas of the gastrointestinal tract can be categorized as LGA (category 3) and high-grade dysplasia (HGD; category 4.1), according to the diagnostic classification of dysplasia established in the revised Vienna classification. Several previous studies^[13,15,16] have classified histopathological diagnoses of SNADETs based on the revised Vienna classification. For the purposes of these studies, LGA was included in the revised Vienna Category 3 (C3), and HGD and superficial adenocarcinoma were included in the revised Vienna Category 4 (C4), such that all C3 lesions were non-malignant, and all C4 lesions were classified as cancer. In this review, only LGA lesions are considered to be sporadic non-ampullary adenomas because LGA lesions show a low risk of progression to adenocarcinoma^[9,13], and non-ampullary duodenal cancers are also considered to be C4 lesions.

The choice of treatment depends on the overall size of a lesion; the depth of its invasion as assessed endoscopically, radiologically, or ultrasonographically; and general factors, such as a patient's age and comorbid conditions. For gastric, esophageal, and non-polypoid colorectal carcinomas that are well differentiated or moderately differentiated and show only minimal submucosal invasion (sm1) without lymphatic involvement, local resection is sufficient. Likewise, for polypoid colorectal carcinomas with deeper submucosal invasion in the stalk/base but without lymphatic or blood vessel invasion, complete local resection is considered adequate treatment^[14,17].

DEFINITION OF SPORADIC NON-AMPULLARY ADENOMA

Duodenal adenomas that do not involve the major duodenal papilla are characterized as benign epithelial tumors of the small bowel. They may occur sporadically or in the context of genetic syndromes, such as familial adenomatous polyposis or Peutz-Jeghers syndrome. A sporadic non-ampullary adenoma is regarded as a precancerous lesion. Previous reports have suggested that there are two carcinogenesis pathways of duodenal cancer: the adenoma-carcinoma sequence and the development of *de novo* cancer^[18-20]. Sporadic non-ampullary adenoma should be differentiated

Table 1 The revised Vienna classification and clinical management

Category	Diagnosis	Clinical management
1	Negative for neoplasia	Optional follow-up
2	Indefinite for neoplasia	Follow-up
3	Mucosal low-grade neoplasia	Endoscopic resection or follow-up
4	Low-grade adenoma	Endoscopic or surgical local resection
	Low-grade dysplasia	
	Mucosal high-grade neoplasia	
	4.1 High-grade adenoma/dysplasia	
	4.2 Noninvasive carcinoma (carcinoma in situ)	
5	4.3 Suspicious for invasive carcinoma	Surgical resection
	4.4 Intramucosal carcinoma	
	Submucosal invasion by carcinoma	

Table 2 Relationship between endoscopic findings and final histological grade

	Category3 (n = 121)		Category4 (n = 275)		P value
Diameter (mean, mm)	11.5 ± 0.7		17.5 ± 0.7		< 0.0001
Location (portion)					
First	23	19%	46	17%	NS
Second	92	76%	205	74%	
Third or fourth	6	5%	24	9%	
Color					
Red	36	30%	124	45%	< 0.01
Isochromatic or white	85	70%	151	55%	
Macroscopic type					
0- I	29	24%	58	21%	NS
0- II a	71	59%	170	62%	
0- II c	21	17%	47	17%	

Color or macroscopic type is adopted from the predominant color when tumor showed multiple colors or macroscopic types. Data from Goda *et al*^[5]. NS: Not significant.

from polyps that occur in genetic syndromes or at the papilla. Polyps are associated with an increased risk of malignancy, and they require different diagnostic and therapeutic strategies than those for sporadic non-ampullary adenomas^[21,22]. Sporadic non-ampullary adenomas account for up to 7% of duodenal polyps that are biopsied using upper endoscopy, which is a prevalence of 1-3 cases per 1000^[3,23]. The mean age at diagnosis is usually in the seventh decade, and the incidence is approximately equal among men and women. The majority of patients are asymptomatic at the time of diagnosis^[24].

DEFINITION OF EARLY NON-AMPULLARY DUODENAL CANCER

Owing to the low prevalence of SNADET, there is no established definition for early non-ampullary duodenal cancer regarding its depth of invasion and risk of lymph node metastasis^[8]. Previous studies have followed the rules that are used for early colorectal^[25] or gastric cancer^[26] and for tumor invasion into the lamina propria, muscularis mucosa (T1a) or submucosa (T1b), regardless of lymph node metastasis^[18,27,28]. There is little information regarding the pathological risk factors for lymph node metastasis of T1a and T1b in non-ampullary duodenal cancer. Nagatani *et al*^[29] found no incidence of lymph node metastasis among 40 pT1a cancers, while Fujisawa *et al*^[27] reported no metastasis among 166 pT1a cancers. The incidence of lymph node metastasis among pT1b cancers was reported to be 5.3%-5.4%^[27,28].

DIFFERENTIAL DIAGNOSIS BETWEEN SNADET C3 AND C4 LESIONS

Characterization using conventional white light imaging
C3 lesions are usually solitary and sessile; and although

they can be located in any part of the duodenum, they are found distally in the majority of patients^[3]. Both C3 and C4 lesions arise most frequently in the second portion of the duodenum, especially in the periampullary area^[18,30,31].

In a Japanese multicenter study, the mean tumor diameter of C4 lesions was significantly larger than that of C3 lesions. C4 lesions were solitary or showed a predominantly red color significantly more frequently than C3 lesions. There were no significant differences between final histological grade and other endoscopic findings, such as tumor location and macroscopic type (Table 2)^[5]. Okada *et al*^[13] showed that a lesion diameter of ≥ 20 mm was significantly predictive of progression to adenocarcinoma. A tumor diameter > 5 mm also seemed indicative for C4 lesion tumors, and this might suggest a recent increase in the number of small C4 lesions of 6-10 mm in diameter^[5]. In addition, out of 139 SNADETs, this case series found 46 mucosal carcinomas (33%) and one submucosal carcinoma that had a tumor diameter of 6-10 mm^[5]. Lesions with a depression component also tended to have a higher cancerous component^[32,33]. Endoscopic features of C4 lesions included a red color in the tumor and a nodular, rough surface^[27,32].

Whitish villus, milk-white mucosa, and white opaque substance

Inatsuchi *et al*^[34] reported that 84% of SNADETs had a whitish villus, which may be helpful in recognizing these lesions under conventional endoscopy. Yoshimura *et al*^[15] showed that 92% of SNADETs had a milk-white mucosa on conventional endoscopy, which is a common endoscopic finding for C3 and C4 lesions. A white opaque substance (WOS) was reported first by Yao *et al*^[35] as a substance in the superficial area of a gastric neoplasia that is visualized in magnifying endoscopy with narrow-band imaging (M-NBI). WOS represents intramucosal accumulation of lipid droplets using oil red O staining^[36]. Tanaka *et al*^[37] suggested



Figure 1 Duodenal adenocarcinoma imaged with magnifying endoscopy with narrow-band imaging. White opaque substance (WOS) in lesion margins on magnifying endoscopy with narrow-band imaging (M-NBI). Speckled WOS is found at the lesion margins (arrows), and little is in the central area.

that whitish villi were a result of lipids in epithelial cells at the villi tips. Whitish villus, milk-white mucosa, and WOS are thought to have the same appearance.

It has been reported that the distribution pattern of milk-white mucosa is classified as either entire or marginal, and the frequency of the marginal type of milk-white mucosa (Figure 1) is significantly higher in C4 lesions compared to C3 lesions^[15]. Whitish villus, milk-white mucosa, and WOS are characteristic of SNADETs, and their individual characteristics may also be useful in differentiating between C3 and C4 lesions.

Characterization using magnifying endoscopy with NBI

NBI is an innovative optical image-enhancing technology that uses narrow blue and green wavelengths to increase the conspicuity of vessels^[38]. M-NBI enables clear visualization of superficial microanatomy and can be used to differentiate between cancerous and non-cancerous lesions of the digestive tract more accurately than conventional endoscopy^[39-44]. However, there have been only a few reports characterizing SNADET using M-NBI.

Yoshimura *et al*^[15] showed that the frequency of a microvascular pattern network type was significantly higher in C4 lesions. Recently, Kikuchi *et al*^[16] have proposed a diagnostic algorithm of M-NBI for SNADET, as shown in Figure 2. They defined vessels that were dilated, tortuous, or had irregular diameter, size, or shape as having an “unclassified pattern”; all C4 lesions had this pattern^[16]. In previous studies, the frequency of an ill-defined mucosal pattern (Figure 3) and mixed-type lesions with multiple surface patterns (Figure 4) were distinctive findings in C4 lesions^[15,16].

Vessel plus surface classification system for magnifying endoscopy with narrow-band imaging

Between December 2008 and January 2015, we retrospectively used ER to investigate both the endoscopic findings and the resected specimens of 64 SNADETs at our hospital. We used the established vessel plus surface (VS) classification system and

Table 3 Comparison of magnifying endoscopy with narrow-band imaging findings according to vessel plus surface classification system and final histological grade in all 64 superficial non-ampullary duodenal epithelial tumors

	Diagnosis from ER specimens				P value
	Category 3 (n = 27)		Category 4 (n = 37)		
Demarcation line	27	100%	37	100%	1
Microvascular pattern; V					
Regular/Absent	10/8	37%/30%	5/17	14%/46%	0.56
Irregular	9	33%	15	41%	
Microsurface pattern; S					
Regular	13	48%	4	11%	0.0008
Irregular	14	52%	33	89%	

ER: Endoscopic resection.

M-NBI to diagnose early gastric cancer^[41], which is the most commonly used system in clinical practice^[42].

We determined whether there was a demarcation line (DL) between a lesion and the background mucosa. Microvascular (MV) patterns and microsurface (MS) patterns were categorized as regular, irregular, or absent. Lesions presenting with an irregular MV pattern with a DL and/or an irregular MS pattern with a DL were diagnosed as cancerous (C4)^[42].

Table 3 shows a comparison of the M-NBI findings for the 64 lesions based on the VS classification. DLs were observed in all of the lesions (100%). There was no significant difference in MV patterns between the C3 and C4 groups. In the SNADETs, there was a tendency for irregular MV patterns to be observed in C3 and C4 lesions. More than 90% of all of the SNADETs in this study demonstrated WOS in the superficial parts of the lesions, obscuring the morphology of subepithelial microvessels in approximately 40% of all lesions. One explanation might be that WOS made it difficult to evaluate the overall distribution and arrangement of microvessels. An irregular MS pattern was present in 14 lesions (52%) in the C3 group and in 33 lesions (89%) in the C4 group, indicating a significant intergroup difference ($P = 0.0008$). An irregular MS pattern was a reliable marker for differentiating between benign and malignant gastric lesions^[40]. Typical cases in the C3 and C4 groups where M-NBI findings were useful for distinguishing between C3 and C4 are shown in Figure 5A-C (C3) and in Figure 6A-C (C4). False-positive cases characterized by malignant M-NBI diagnoses and benign pathological diagnoses are shown in Figure 7A-C. We found that an irregular MS pattern was significantly more frequent in the C4 group, while there was no significant difference in MV patterns between the C3 and C4 groups. These findings may be useful in distinguishing between carcinomas and benign lesions in SNADETs. However, the additional advantages of M-NBI remain unclear, and further studies, including ones on the relationship between histopathological type and MS findings, are

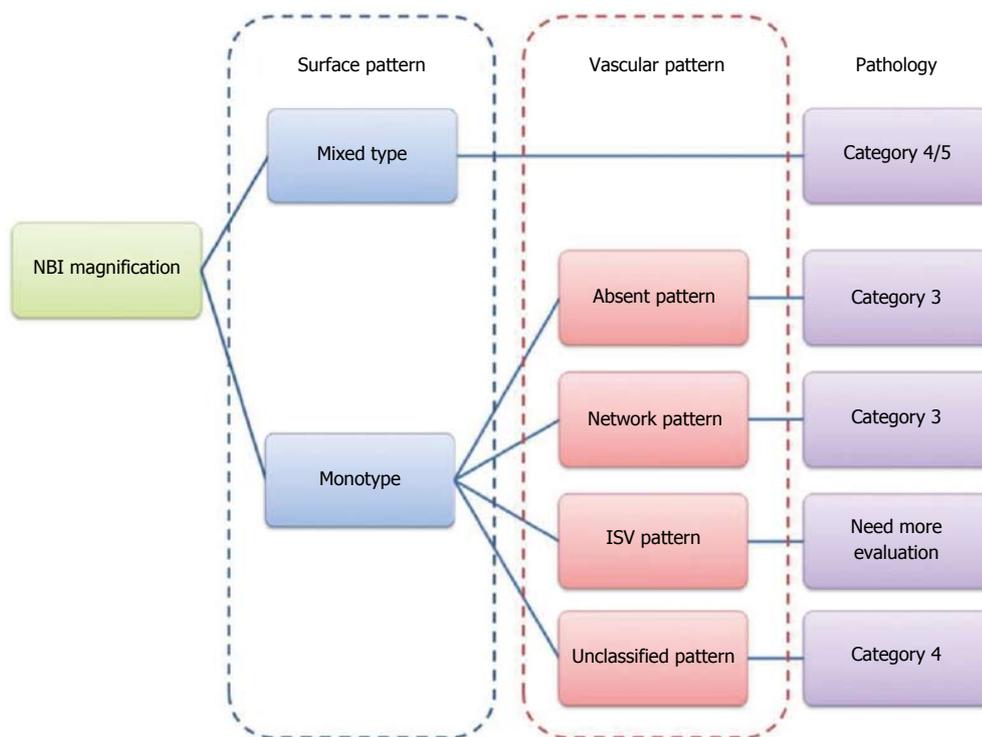


Figure 2 Diagnostic algorithm of magnifying endoscopy with narrow band imaging for superficial non-ampullary duodenal epithelial tumor. From Kikuchi *et al.*^[16]



Figure 3 Duodenal adenocarcinoma imaged with magnifying endoscopy with narrow-band imaging. An indistinct area of a marginal crypt epithelium (MCE) structure as imaged by magnifying endoscopy with narrow-band imaging (M-NBI). There are no discernible microsurface features (yellow circle).



Figure 4 Duodenal adenocarcinoma imaged with magnifying endoscopy with narrow-band imaging. Because of uneven distribution of white opaque substance (WOS) on magnifying endoscopy with narrow-band imaging (M-NBI), this lesion displays multiple microsurface patterns as mixed-type (yellow circle).

required to clarify these issues.

Magnifying chromoendoscopy

Chromoendoscopy was introduced to improve the success of duodenal polyp detection and differentiation^[45,46]. Chromoendoscopy in combination with magnifying endoscopy is useful in distinguishing neoplastic from non-neoplastic colorectal polyps^[47]. It has been important to show that magnifying endoscopy combined with chromoendoscopy is useful to discriminate between neoplastic and non-neoplastic colonic polyps, based on the pit-pattern classification^[48-51]. Endo *et al.*^[1,52] diagnosed patients with sporadic non-ampullary adenoma or non-

ampullary duodenal cancer based on magnified images that were stained with crystal violet through the use of the pit-pattern classification for colonic mucosa. Using magnification endoscopy, they categorized SNADETs into convoluted, leaf-like, reticular/sulciolar, and colon-like patterns^[1,52].

Preoperative diagnosis using biopsy

Okada *et al.*^[13] analyzed 68 sporadic non-ampullary duodenal adenomas that were diagnosed using biopsy and reported that LGA lesions show a low risk of progression to adenocarcinoma, whereas HGD lesions show a high risk of progression to adenocarcinoma. In a preoperative diagnosis, accurately differentiating

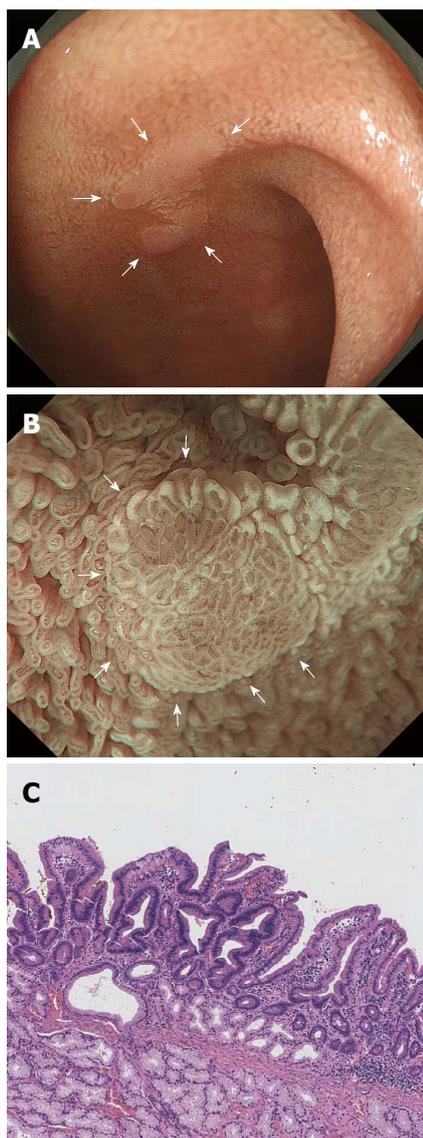


Figure 5 Magnifying endoscopy with narrow-band imaging of a duodenal adenoma. A: Endoscopic findings using conventional endoscopy with white light imaging. A pale, slightly elevated lesion (10 mm in diameter, arrow) is observed in the proximal duodenum; B: Endoscopic findings using magnifying endoscopy with narrow-band imaging (M-NBI). A demarcation line (DL, arrows) separates changes in the mucosal microsurface (MS) structure from the surrounding normal mucosa. Vessel plus surface (VS) classifications: V, Because of the white opaque substance (WOS), the morphology of the subepithelial microvessels cannot be observed, making this an absent microvascular (MV) pattern; S, The WOS has a regular reticular pattern with a symmetrical distribution and regular arrangement. Thus, this lesion is graded as a regular MS pattern using WOS as a marker for the MS pattern. The VS classification of this lesion was absent MV pattern and regular MS pattern (WOS+) with a DL. Therefore, the M-NBI diagnosis was benign; C: The final histological diagnosis was of a low-grade adenoma.

cancer from adenoma is difficult based on biopsy findings alone. Forceps biopsy is recommended for all suspect lesions, although 15%-56% of cancers may be missed at biopsy due to sampling error compared with using surgically resected specimens^[53,54]. In a multicenter study, the sensitivity, specificity and accuracy of preoperative diagnosis using biopsy for

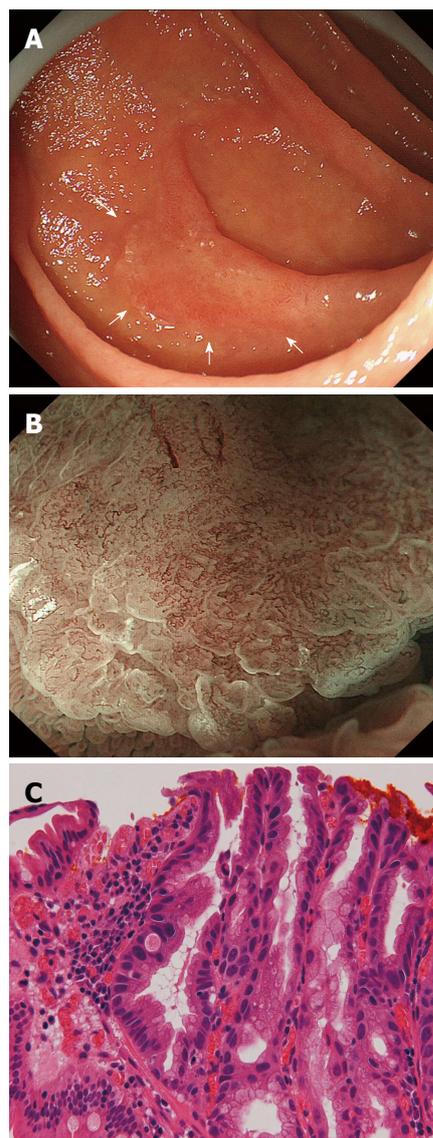


Figure 6 Duodenal adenocarcinoma with typical magnifying endoscopy with narrow-band imaging findings. A: Endoscopic findings using conventional endoscopy with white light imaging. A reddish, slightly elevated lesion (13 mm in diameter, arrows) is observed in the second portion of the duodenum; B: Endoscopic findings using magnifying endoscopy with narrow-band imaging findings (M-NBI). A clear demarcation line (DL) is visible because of differences in the vessel plus surface (VS) component between the cancerous and noncancerous mucosa. V: Proliferation of microvessels with variable sizes, asymmetrical distribution and irregular arrangement make this an irregular microvascular (MV) pattern; S: There are areas where the marginal crypt epithelium (MCE) cannot be visualized and where the visible MCE shows a variety of morphologies, an asymmetrical distribution and an irregular arrangement. This lesion is assessed as an irregular mucosal microsurface (MS) pattern. The VS classification of this lesion was an irregular MV pattern and irregular MS pattern with a DL. Therefore, the M-NBI diagnosis was cancer; C: The final histological diagnosis was a well-differentiated intramucosal adenocarcinoma.

final HGD and superficial adenocarcinoma histology were 58%, 93%, and 68%, respectively^[5]. In another study, T1a cancer was observed in 13.5% of patients in whom initial biopsies indicated simple adenomas^[55]. Owing to the thinness of the duodenal wall, the biopsy procedure itself may induce unintended fibrosis

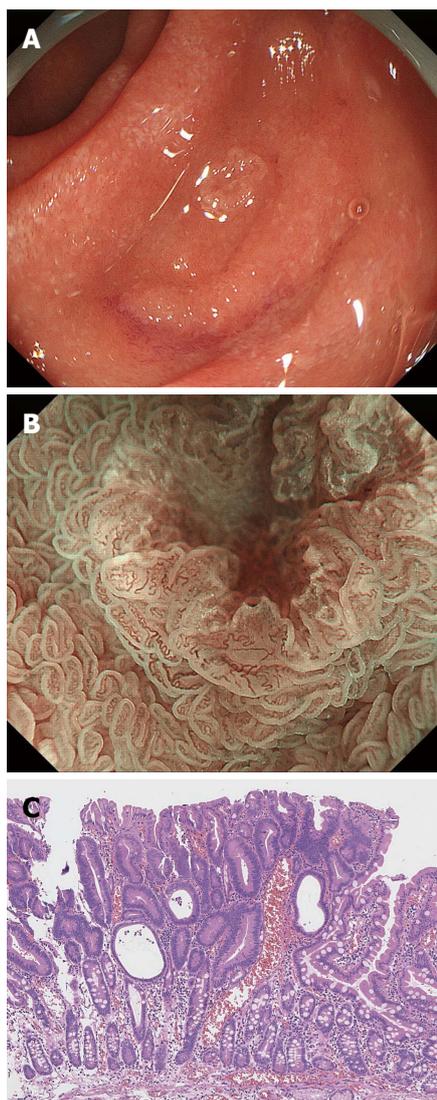


Figure 7 False-positive magnifying endoscopy with narrow-band imaging diagnosis. A: Endoscopic findings using conventional endoscopy with white light imaging. A whitish, slightly depressed lesion (5 mm in diameter) is observed in the second portion of the duodenum. In this case, magnifying endoscopy with narrow-band imaging diagnosis (M-NBI) examination was conducted before biopsy; B: Endoscopic findings using M-NBI. A clear demarcation line (DL) is visible because of differences in the vessel plus surface (VS) component between the tumor and surrounding mucosa. V: The individual vessels show a variety of morphologies, such as open- and closed-looped and coil-shaped, with no two microvessels sharing the same morphology. The microvessels are anastomosing with each other within the intervening parts but show no consistent regularity. Therefore, this lesion was assessed as an irregular microvascular (MV) pattern; S: This individual section of marginal crypt epithelium (MCE) shows a curved morphology but lacks continuity or a consistent directionality, and the intervening parts are also irregular with unequal sizes. Therefore, this lesion was assessed as an irregular mucosal microsurface (MS) pattern. The VS classification of this lesion was an irregular MV pattern and irregular MS pattern with a DL. Therefore, the M-NBI diagnosis was cancer; C: The final histological diagnosis was a low-grade adenoma.

associated with a lesion, which may complicate subsequent ER^[10]. Consequently, it is necessary to perform a biopsy while causing a minimal amount of damage, and ER as a diagnostic therapy should be considered in some cases that are endoscopically diagnosed as carcinoma.

Confocal laser endomicroscopy and autofluorescence imaging

In recent years, many new imaging modalities have been developed and explored for use in the real-time diagnosis of duodenal lesions^[56-58]. Confocal laser endomicroscopy (CLE) is a powerful technology that provides magnification $\times 1000$ imaging using intravenous fluorescein as a contrast agent^[59]. Currently, there are two types of CLE: probe-based CLE (pCLE) and endoscopic-based CLE (eCLE)^[60]. In a recent study, pCLE was used along with NBI (GIF H-180; Olympus) for duodenal adenoma diagnosis, and it was concluded that pCLE provided better sensitivity than NBI (92% vs 83%, $P = 0.8$); duodenal adenoma diagnosis criteria for pCLE and NBI in this study were based on Barrett's esophagus criteria^[58]. Pittayanon *et al*^[61] reported that the diagnostic criteria for duodenal non-adenomatous and adenomatous lesions using pCLE were normal epithelium border with regular capillary pattern and dark/irregular/non-structural mucosa with normal or abnormal capillary networks, respectively. Autofluorescence imaging (AFI) is an endoscopic technique that uses autofluorescence that is emitted from an endogenous fluorophore following exposure to short-wavelength photoexcitation^[62]. AFI has not been used to evaluate duodenal and periampullary lesions. Many new imaging modalities seem to be useful, but because of insufficient data on this uncommon entity, a large multicenter study is required to support this concept.

ENDOSCOPIC DIAGNOSIS OF SNADET EXTENT AND INVASION DEPTH

Determining SNADET margins using conventional endoscopy is easy, as it is similar to detecting epithelial tumors of the colon or rectum^[1]. However, it is difficult to differentiate T1a from T1b non-ampullary duodenal cancer using barium studies or endoscopy^[27]. Central dimpling or ulceration observed during endoscopy suggests invasive carcinoma^[63]. Several previous studies have classified morphological types of superficial SNADETs based on the classification criteria that are used for colorectal tumors^[20,27,28]. Macroscopic types based on endoscopic features include the protruded pedunculated (Ip), protruded sessile (Is), and semipedunculated (Isp) types and the superficial elevated (II a), flat (II b), and superficial shallow or depressed (II c) types^[26]. Previous studies showed that 0-I or 0-II a + II c macroscopic types with a red color were usually endoscopic features of submucosal carcinoma^[5,29]. Endoscopic ultrasonography (EUS) is accurate in diagnosing gastrointestinal abnormalities because of its ability to image intestinal wall architecture and its surrounding structures in detail^[64]. Tio *et al*^[65] reported that EUS is accurate in diagnosing duodenal sessile villous adenomas, and it is, therefore, useful in planning treatment. EUS helps to evaluate larger lesions (greater than 2 cm

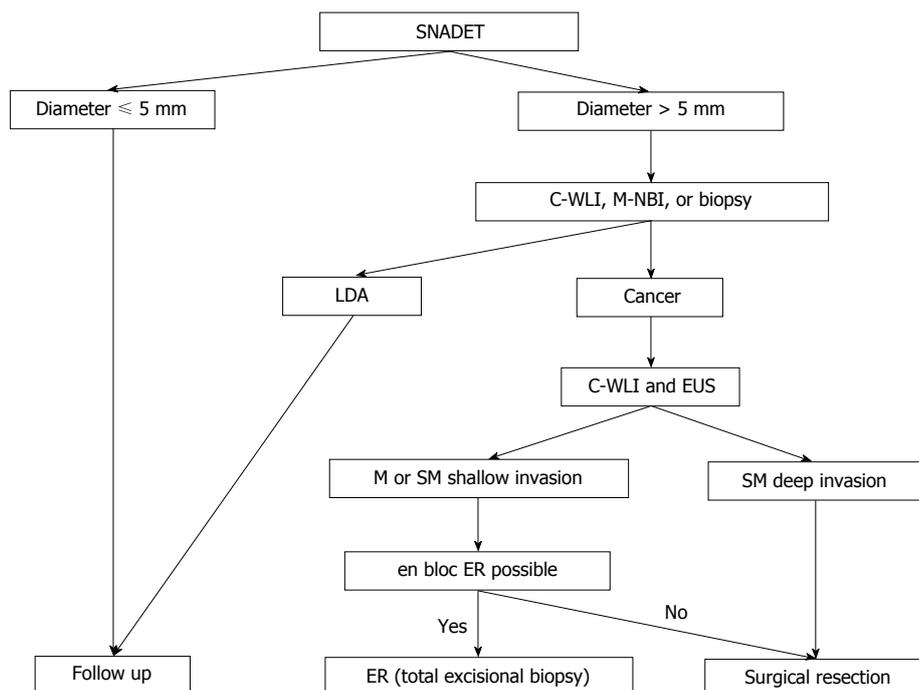


Figure 8 Suggested algorithm for the management of superficial non-ampullary duodenal epithelial tumor according to depth of invasion; tumor size; endoscopic findings, including magnifying endoscopy; and biopsy results. Endoscopic features of cancer are a red color in the tumor; a nodular, rough surface on conventional white light imaging; a marginal type of milk-white mucosa; an unclassified vascular pattern; a frequency of ill-defined mucosal pattern; and a population of mixed-type lesions with multiple surface patterns on magnifying endoscopy with narrow-band imaging. Endoscopic features of submucosal carcinoma are ulceration and a 0-I or 0-II a + II c macroscopic type with a red color. SNADET: Superficial non-ampullary duodenal epithelial tumor; C-WLI: Conventional white-light imaging; M-NBI: Magnifying endoscopy with narrow-band imaging; LDA: Low-grade adenoma; EUS: Endoscopic ultrasonography; ER: Endoscopic resection.

in size) to establish the relationship of a duodenal polyp to the pancreatobiliary tree and to determine endoscopic resectability when biopsy specimens have shown HGD^[66]. Preoperative EUS for six submucosal carcinomas enabled the prediction of submucosal invasion with 67% accuracy^[5].

CONCLUSION

From this review, a suggested algorithm for the management of SNADET is shown in Figure 8. Given the heterogeneity of the lesions and the patient population, it is difficult to set guidelines that would encompass all possible scenarios, so each case must be taken on an individual basis. Because the incidence of SNADET is extremely rare, endoscopic findings that suggest early non-ampullary duodenal cancer have not yet been established. As indications for endoscopy increase and as techniques evolve, the rate of duodenal adenoma and duodenal adenocarcinoma detection, especially of small lesions, will likely increase. Newer endoscopic techniques, including magnifying endoscopy, may help to guide these diagnostics, but their additional advantages remain unclear, and further studies are required to clarify these issues.

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