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Morphological classifications of gastrointestinal lesions

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A B S T R A C T

In the era of spreading adoption of gastrointestinal endoscopy screening worldwide, endoscopists encounter an increasing number of complex lesions in the gastrointestinal tract. For decision-making on optimal treatment, precise lesion characterization is crucial. Especially the assessment of potential submucosal invasion is of utmost importance as this determines whether endoscopic removal is an option and which technique should be used. To describe a lesion and stratify for the risk of submucosal invasion, several morphological classification systems have been developed. In this manuscript, we thoroughly discuss a systematic approach for the endoscopic assessment of a lesion, which include location, size, Paris classification, lateral spreading tumor classification if applicable and evaluation of the surface pattern with advanced endoscopic imaging techniques. The use of advanced imaging techniques improves the characterization of mucosal surface patterns and helps to determine whether lesions are amenable to endoscopic resection.

Systematic and structured reporting

Over the last decades, optimization of gastrointestinal endoscopy has markedly improved the detection, characterization and treatment of lesions located throughout the gastrointestinal tract. Colonoscopy is widely used for screening and surveillance aiming to reduce morbidity and mortality from colorectal cancer (CRC), as it permits both detection and removal of neoplastic lesions [1]. The efficacy of colonoscopy however, depends on the quality of the exam. In an effort to improve the quality of colonoscopy, several key quality indicators have been investigated in its relation with post-colonoscopy cancers [2–4]. Accordingly, systematic registration of these quality indicators in clinical practice has recently been endorsed by professional societies [5,6]. Reporting these indicators is ideally facilitated by a structured colonoscopy reporting system, generating standardized and complete reports [7,8]. These standardized reports can be used to measure the quality of the exam and can also be linked to clinical outcomes.

The same accounts for the assessment of resection techniques. Previous studies have revealed the importance of adequate and complete resection of neoplastic lesions to prevent post-colonoscopy cancers [9–11]. To compare the outcomes of removal of neoplastic lesions, structured description of the resected lesion and the technique used are crucial. Systematic follow-up and endoscopic inspection for residual tissue or post-colonoscopy cancers can then be linked to the removal. Ideally, such a structured description is also performed for lesions that were not removed during colonoscopy because they were considered harmless. Detailed description of endoscopic findings will also facilitate optimal assignment of appropriate surveillance intervals.

The aim of this review is to provide an evidence-based framework for a structured endoscopic evaluation of colonic lesions in order to decide the optimal treatment of these lesions. Therefore we systematically searched PUBMED, EMBASE, the Cochrane database and sites of (inter)national societies for English written

Abbreviations: ESD, Endoscopic submucosal dissection; ESD, endoscopic mucosal resection; ESGE, European Society of Gastrointestinal Endoscopy; BSG/ACPGBI, British Society of Gastroenterology/Associations of Coloproctologists of Great Britain and Ireland; JES, Japan Esophageal Society; ASGE, American Society of Gastrointestinal Endoscopy; CRC, colorectal cancer; LST, laterally spreading type; NICE, NBI international colorectal endoscopic; NBI, narrow band imaging; JNET, Japanese NBI expert team.

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literature or guidelines using the keywords “location”, “size”, “morphology”, “surface pattern”, “Paris classification”, “lateral spreading type”, “invasive cancer”, “polyps”, “endoscopic mucosal resection”, “endoscopic submucosal dissection” and “endoscopic treatment”. Additional references were obtained from bibliographies of the identified articles. The reporting and treatment approaches proposed in this review are in line with those proposed in the international practice guidelines of European Society of Gastrointestinal Endoscopy (ESGE), British Society of Gastroenterology/Associations of Coloproctologists of Great Britain and Ireland (BSG/ACPGBI), Japan Esophageal Society (JES) and American Society of Gastrointestinal Endoscopy (ASGE).

Importance of predicting risk of submucosal invasion

Neoplastic lesions are the result of abnormal cell proliferation and are benign when they are confined to the mucosa. When the lesions invade into the submucosa or beyond they are considered malignant and acquire the potential to spread through the lymphatic system and blood vessels and cause metastases. Definitive exclusion of invasive growth in a lesion can only be established at histopathology after adequate endoscopic or surgical resection. On-site decision-making on treatment requires real-time prediction of the possibility of growth into the submucosa. In the past decade, the endoscopic armamentarium has been extended by piecemeal endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), and these techniques are increasingly used as endoscopic treatment options to prevent more invasive surgery [12,13]. However, when invasion is beyond the mucosa, endoscopic resection has risks and might not be curative. Early CRC with invasive growth confined to the submucosa (pT1 carcinoma) has a risk of lymph node metastases of 7–20% [14,15]. The risk of lymph node metastases is related to many factors, including the size of the tumor, the histopathological depth of invasion (Kikuchi and Haggitt-level), presence of lymphovascular invasion, and specific tumor biology including differentiation grade and level of tumor budding [16–18]. In the case of early cancers, piecemeal EMR impairs a definite diagnosis as the completeness of the resection and depth of invasion are difficult to judge. ESD overcomes this important limitation of piecemeal EMR as it provides en-bloc resection in which the resection margins can be assessed for invasive growth. If histopathological evaluation reveals a high risk of lymph node metastases, an additional oncological resection for histological evaluation of the draining lymph nodes is usually advised.

Data on survival benefits of either surgical or endoscopic treatment of CRCs confined to the submucosa are limited [19–21]. The following studies describe retrospective observational cohorts in which many factors may have contributed to the decision for primary surgery or endoscopic treatment. In a population-based database study, the adjusted 5-year survival was similar for surgically resected pT1 cancers diagnosed without lymph node metastases compared to endoscopically resected early submucosal invasive cancers treated without additional surgery [19]. Endoscopic treatment was associated with older age, more comorbidity and well-differentiated CRCs. Information on the presence of lymphovascular invasion and radical excision margins was unavailable. In a single-center study, 93 patients with early submucosal invasive well-differentiated rectal cancers without lymphovascular invasion had high tumor-free (92%) and tumor-related (98%) survival when radical en-bloc treatment with transanal endoscopic microsurgery was performed [20]. In addition to the latter, endoscopic resection before surgical resection of pT1 CRCs with one or more histological risk factors for lymph node metastases was not associated with an increased rate of lymph node metastases at surgical resection or increased local and distant recurrence rates during follow-up [21]. The outcomes of these studies suggest that complete endoscopic resection is an appropriate treatment for early invasive lesions with growth confined to the submucosa and in absence of other high-risk features.

Structured reporting of neoplastic lesions

Location

The systematic approach starts with the description of the location of the lesion. Endoscopic resection of lesions located in the proximal colon is associated with increased risks. The colonic wall of the caecal pole is the thinnest and has the highest risk for post-procedural complications like bleeding and perforation [22,23]. Removal of lesions located in the rectum, where the colonic wall is thickest, is easier, safer and, due to the easy accessibility, these lesions are amenable to other non-invasive treatment options like ESD, TEM or TAMIS [24]. Polyps that cross two folds, are located behind a fold, have a ‘clamshell’ distribution around a fold, are located peri-diverticular, peri-appendicular or at the linea dentata and those with involvement of the ileocecal valve tend to be more difficult to remove endoscopically and have a higher risk of incomplete removal [25]. In line with the recent ESGE guideline, we suggest to refer patients with complex located lesions (ileocecal valve, peri-appendicular or peri-diverticular) to an expert setting for evaluation of endoscopic therapy [26].

Size

The size of colonic lesions is directly related to the risk of cancer [27–29]. One to 5 mm (diminutive) colonic lesions have a very low risk of harboring invasive growth: 0–0.1% [27]. For 6–9 mm lesions, this risk ranges between 0 and 0.4% [27]. For lesions of 10 mm and larger, the risk of cancer gradually increases from 2.4% for 10–20 mm lesions to a maximum of 19.4% for polyps measuring more than 20 mm in size [28]. When considering endoscopic treatment, the maximum size for safe removal with en-bloc snare resection is approximately 20 mm. For larger lesions and the smaller ones not amenable for en-bloc resection, piecemeal EMR is a treatment option if no morphological signs of submucosal invasion are present. In those cases ESD could be considered as treatment option [24,26].

Although polyp size is an important determinant for decision-making in treatment, it is based on subjective endoscopic estimates as no gold standard is available. Histopathological assessment of lesion size is also subject to bias and interobserver variability. In a study comparing endoscopic to histopathologic sizes, half of the polyps that were estimated by the endoscopist as sized at least 1 cm fell below this threshold based on pathology measurements [30]. Even when a visual cue of a known diameter was placed adjacent to lesions of exact size in ex-vivo studies, only 33–37% of measurements were exact to the millimeter [31,32]. Recently, a new polyp measurement technique was introduced aiming to reduce this inter- and variability [32]. The technique provides a 1×1 mm measurement grid implemented in the endoscope view. In an ex-vivo study with 50 expert endoscopists, 1–10 mm lesions were evaluated against this visual grid cue and measurement was accurate in 90% of cases. This technique deserves real-time study and might also be suitable for implementation in new endoscopy software. Until then, we suggest to size a lesion before resection with an open snare of a known diameter or a biopsy forceps.

Paris classification

As polyp morphology might have a predictive value for the presence of invasive growth, a group of Western and Japanese

endoscopists, pathologists and surgeons established an endoscopic classification scheme describing polyp morphology for superficial neoplastic lesions in the esophagus, stomach and colon [33]. This Paris classification divides polyps into several categories depending on their endoscopic shape: pedunculated (0-Ip), sessile (0-Is), slightly elevated (0-IIa), flat (0-IIb), slightly depressed (0-IIc) and excavated (0-III) (Fig. 1). Depressed morphology is rare, it was diagnosed in 1.0% of more than 1800 neoplastic lesions in a prospective study of Soetikno et al. [34]. Remarkably, one-third of these depressed lesions contained invasive growth. In the Australian ACE study, outcomes of 479 piecemeal EMRs were prospectively registered [35]. Of those, 22 lesions had a depressed component and 7 (32%) of these had submucosal invasion on histopathology [35]. Lesions with excavated morphology have a very high risk of invasive cancer, but seem extremely rare in the colon [33]. Western studies describing these lesions are missing. Flat lesions (IIa, IIb, IIc), also called nonpolypoid lesions, are relatively common and are associated with a greater risk of harboring high-grade dysplasia or (early) CRC than polypoid (Ip and Is) lesions in some studies [34,36–38], while other studies do not show such an increased risk [39–41]. These conflicting results might be caused by interobserver variability among endoscopists in assessing polyp morphology. In a recent study among international expert endoscopists, only a moderate interobserver variability for the Paris Classification was demonstrated [42]. The proportion of polyps assessed as *flat* by the experts ranged from 13% to 40% [42]. As even experts were not able to uniformly differentiate these lesions, these findings suggest that studies describing the prevalence and corresponding histological outcomes of polypoid and non-polypoid lesions should be interpreted with caution. Therefore, instead of artificially classifying polyps into a polypoid or nonpolypoid group, we believe that it is more important to put effort in identifying depressed lesions or depressed parts in a lesion (0-IIC), as these polyps might have invasive growth [33,34,38,43].

Laterally spreading type classification

The term 'laterally spreading type' (LST) lesion refers to lesions with a lateral growth of at least 10 mm [44]. The LST classification is used beside the Paris classification to stratify these larger lesions for the risk of invasive growth. LSTs are subdivided into granular and non-granular types. The granular type consists of homogeneous or nodular-mixed morphology while the non-granular type is flat-elevated or pseudo-depressed (Table 1). The frequency of submucosal invasion increases with size and this is independent of the individual sub-classification [35,45–47]. The non-granular type is associated with an increased frequency for harboring invasive cancer [35,45]. In a study from Japan including 511 LSTs, non-granular LSTs with a median size of 16 mm twice as often demonstrated invasive growth when compared to granular LSTs (14% vs 7%, p<0.01) [46]. These findings were confirmed by another study by Oka et al in which 1,363 LSTs with a median size of 23 mm were described [47]. Non-granular LSTs with a pseudo-depressed component more often demonstrated submucosal invasion (42%) compared to flat-elevated LSTs (6%, $p < 0.01$). For granular LSTs, the presence of a large dominant nodule >10 mm in size was also strongly associated with an increased frequency of submucosal invasion [46,48].

Table 1
Laterally spreading tumor (LST) classification [44].

Subtypes of LST	Corresponding Paris classification
Granular LST	
Homogenous type	0-IIa
Nodular mixed type	0-IIa, 0-IIa + Is
Non-granular LST	
Flat elevated type	0-IIa, 0-IIb
Pseudo-depressed type	0-IIa + IIc

When considering the LST classification, both non-granular LSTs as well as granular LSTs with a large dominant nodule of at least 10 mm exhibit the greatest risk of invasive cancer. These lesions warrant careful evaluation of mucosal surface pattern for signs of deep submucosal invasion prior to treatment and should preferably be removed en-bloc.

Mucosal surface pattern

The introduction of high-definition endoscopes in clinical practice has improved detection rates of neoplastic lesions when compared to standard definition [49,50]. These high-definition endoscopes also allow for critical evaluation of mucosal surface characteristics with or without the application of a topical dye. The latter technique is called chromoendoscopy in which topical application of methylene blue or indigo carmine is used to highlight the mucosal pit pattern. In addition, almost all available endoscopes and endoscopy processors contain built-in digital chromoendoscopy techniques, which can be activated by a simple push on a button of the endoscopic handle. These techniques use selective light filters to enhance mucosal and vascular details. Several optical classification systems have been validated for both chromoendoscopy and digital chromoendoscopy, either with or without zoom magnification (Table 2). These classifications aim to predict the lesion histology and the risk of invasive growth by evaluation of mucosal surface details.

The *Kudo classification* was originally established to describe the micro-architecture of epithelial pits, the so-called pit pattern, during zoom magnification chromoendoscopy [51]. The classification was described in 1994. Multiple Western research groups have used the classification system for endoscopic prediction of polyp histology using several digital chromoendoscopy techniques and achieved high accuracies and good inter-observer agreement without using zoom magnification chromoendoscopy [52–55].

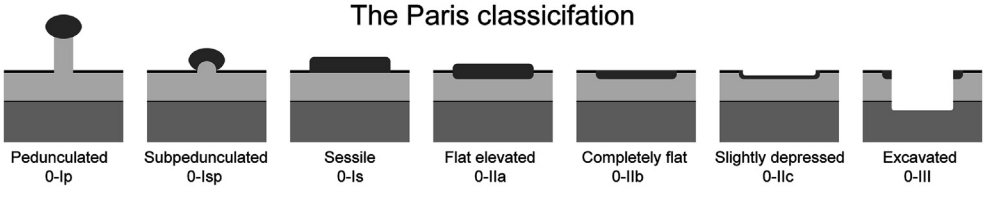

Fig. 1. Schematic representation of the Paris classification for mucosal neoplasia. Lesion morphology is broadly divided into protruded, flat elevated, and flat morphologies. Protruded lesions rise ~2.5 mm above the surrounding mucosa and include pedunculated (0-Ip), subpedunculated (0-Isp), and sessile (0-Is) types. Flat elevated lesions (0-IIa) rise ~2.5 mm above the surrounding mucosa, and features such as central depression (0-IIa or c) or a broad based nodule (0-IIa or Is) are described. Flat lesions include 0-IIb (barely perceptible elevation), 0-IIc (depressed), and 0-III (excavated) types.

Table 2
Overview of surface pattern classifications designed to distinguish between superficial and deep submucosal invasion [51,60,61,65–67].

Classification name	Type of image-enhanced endoscopy used	Morphological feature	Lesions confined to mucosa	Lesions with superficial submucosal invasion	Lesions with deep submucosal invasion
Kudo [51]	Dye-spray (magnifying) chromoendoscopy	Pit pattern	Asteroid or star-shaped pit pattern (II) Tubular or round pit pattern with regular or branched pits (IIIS or IIIL) Gyrus-like pit pattern (IV)	Irregular aggregated type IIIS, IIIL or IV pits (Vi pit pattern)	Non-structured, amorphous or areas with loss of pit pattern (Vn pit pattern)
NICE [60,61]	NBI	Color	Same or lighter (type 1) Brown (type 2)	NA	Brown to dark brown (type 3)
		Vessels	None or isolated lacy vessels (type 1) Brown vessels surrounded by white pits (type 2)	NA	Areas with disrupted vessels (type 3)
		Surface pattern	Dark or white uniform spots (type 1) Tubular or branched (type 2)	NA	Amorphous or absent pattern (type 3)
Sano [65]	Magnifying NBI	Vessels	No capillary vessels present (type I) Presence of feshed capillary vessels surrounding mucosal glands (type II)	Presence of broad irregular meshed capillary vessels with lack of uniformity and branching (Type IIIA)	Absence of vascularity or presence of loose micro capillary vessels (type IIIB)
Hiroshima [66]	Magnifying NBI	Vessels	Absence of vessels or lacy isolated vessels (type A) Regular meshed microvessels (type B)	Homogenous thickness and distribution of vessels (type C1) Heterogeneous thickness and distribution of vessels (type C2)	Avascular areas and fragments of scattered microvessels (type C3)
		Surface pattern	Brown or black dots, star or round shaped pits surrounded by white (type A) Regular surface pattern with vessels surrounding the pits (type B)	Irregular surface pattern (type C1) More irregular surface pattern due to increased microvessel intensity (type C2)	Completely unclear surface pattern (type C3)
JNET [67]	Magnifying NBI				
		Vessel pattern	Absent (type 1) Regular caliber and distribution of vessels (type 2A)	Variable caliber of vessels with irregular distribution (type 2B)	Areas with loose vessels and interruption of thick vessels (type 3)
		Surface pattern	Regular dark or white spots similar to surrounding normal mucosa (type 1) Regular tubular, branched or papillary surface pattern (type 2A)	Irregular or obscure surface pattern (type 2A)	Areas with amorphous surface pattern (type 3)

Classification of the pit-pattern is designed to differentiate between non-neoplastic, adenomatous and cancerous lesions. Whereas Kudo type I and II are associated with non-neoplastic mucosa, type IIIS/L and IV are associated with adenomatous histology and a Kudo type V pit pattern might indicate cancer. In the Australian ACE study, 56% of the lesions demonstrating a Kudo V pit pattern harbored submucosal invasion compared to 4–5% for type III and IV ($p < 0.001$) [35]. In an effort to discriminate the depth of invasion of a type V lesion, Kudo subtypes Vi and Vn were created for differentiation between superficial and deep submucosal invasion with zoom magnification chromoendoscopy, respectively [56–59]. Type Vi represents pit pattern similar to type IIIS/L or IV with irregular arrangement of the surface pattern. A Type Vn pit pattern is defined as a pattern with obvious non-structure of pits. In a prospective real-time study with Japanese experts using zoom magnification chromoendoscopy, the reported sensitivity, specificity and diagnostic accuracy of type Vi and Vn to differentiate superficial submucosal invasive cancer from deep invasive cancer were 86%, 99% and 99%, respectively [59]. However, we suggest not using these subtypes Vi and Vn in daily practice as these have not been validated in daily practice outside of Japan and require additional need of topical dyes and zoom magnification colonoscopes.

The *NBI international colorectal endoscopic (NICE) classification* for narrow band imaging (NBI) was initially designed and validated to make an optical diagnosis using NBI without zoom magnification to differentiate between hyperplastic (NICE 1) and adenomatous (NICE 2) lesions [60]. Examination of the surface characteristics of a lesion is based on color, vessels and surface pattern. An update of the NICE-classification also included surface characteristics for deep submucosal invasive cancer (NICE 3) [61]. In an image-based validation study of this updated NICE-classification, medical students received training and were shown multiple still images of colorectal lesions. This training resulted in a high overall sensitivity and negative predictive value of 92% for high-confidence predictions of deep submucosal

invasive cancer. In addition, the interobserver agreement for predicting deep submucosal invasive cancer was substantial (kappa 0.70). Previous studies have shown that the NICE classification is easy to learn, although these focused on the earlier classification differentiating between hyperplastic and adenomatous polyps [62,63]. For endoscopic differentiation between hyperplastic and sessile serrated lesions, the Dutch 'Workgroup serrated polypS and Polyposis' (WASP) classification combined the NICE classification (type 1 and 2) with four endoscopic features of sessile serrated lesions [64]. In an image-based validation study, the WASP classification achieved good accuracies for differentiating between sessile serrated, hyperplastic lesions and adenomatous lesions.

In Japan, three other classification systems for NBI plus zoom magnification have been proposed. These include the *Sano classification*, the *Hiroshima classification* and the *Japan NBI Expert team* (*JNET*) *classification* [65–67]. These classifications take both surface structure and vascular patterns into account. For treatment decisions, these classifications provide subclassifications to endoscopically differentiate between superficial and deep submucosal invasion. However, requirement of zoom magnification colonoscopies, additional need of topical chromoendoscopy agents and lack of validation outside Japan currently limit the usability of the Sano, Hiroshima and JNET classification.

To determine whether lesions are suitable for endoscopic resection, the outcomes of a recent systematic review support the use of digital or dye-spray chromoendoscopy to evaluate mucosal features of submucosal invasion [68]. The use of NBI or zoom magnification chromoendoscopy yielded higher sensitivity for prediction of invasive growth and deep submucosal invasion compared to gross morphological features alone. As there is considerable overlap between the previously mentioned classifications and none of these have been compared in real-time directly, either one can be used. In line with the recent BSG and ESGE guideline, we suggest using the NICE and/or Kudo classification with high-definition digital chromoendoscopy techniques as they have shown good inter-observer agreement and can be easily

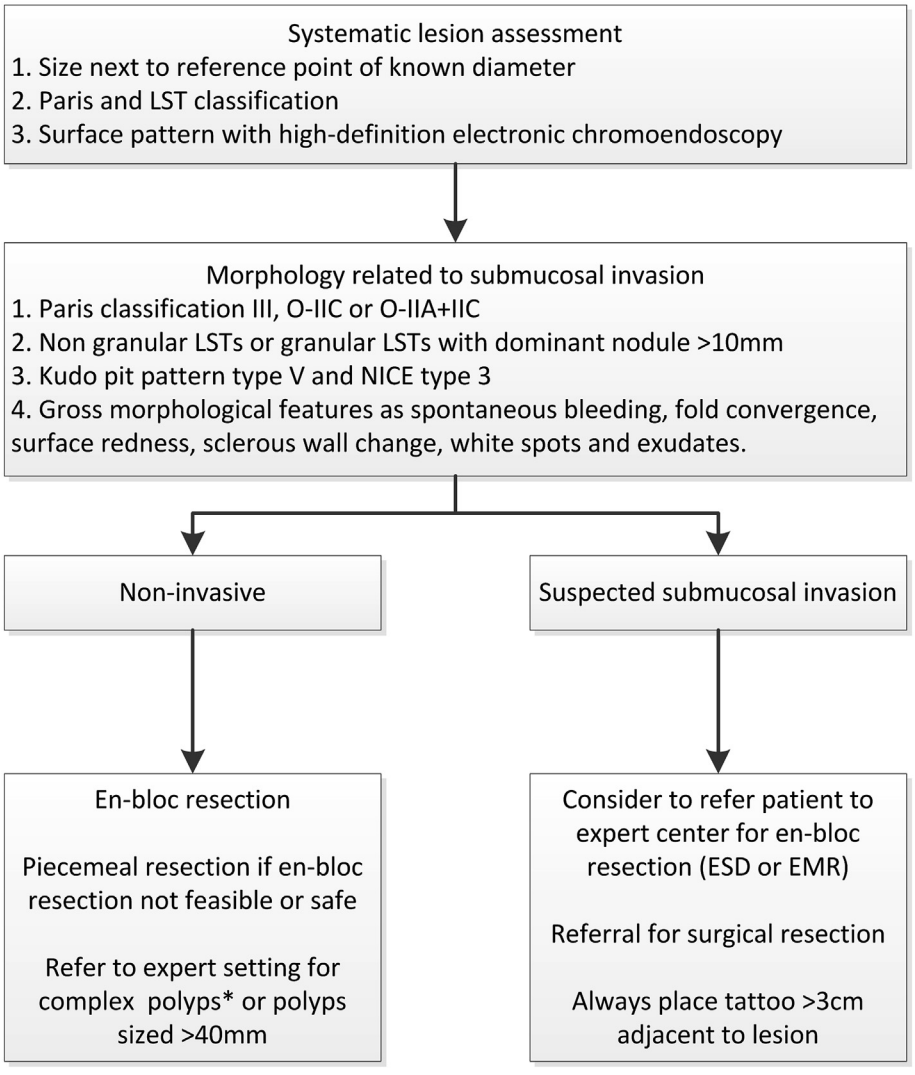

Fig. 2. Recommended flowchart for endoscopic lesion assessment and subsequent treatment approach for colorectal polyps. *Complex lesions are lesions with difficult location (i.e. ileocecal valve, peri-appendiceal, peri-diverticular or ileorectal junction) or non-lifting sign.

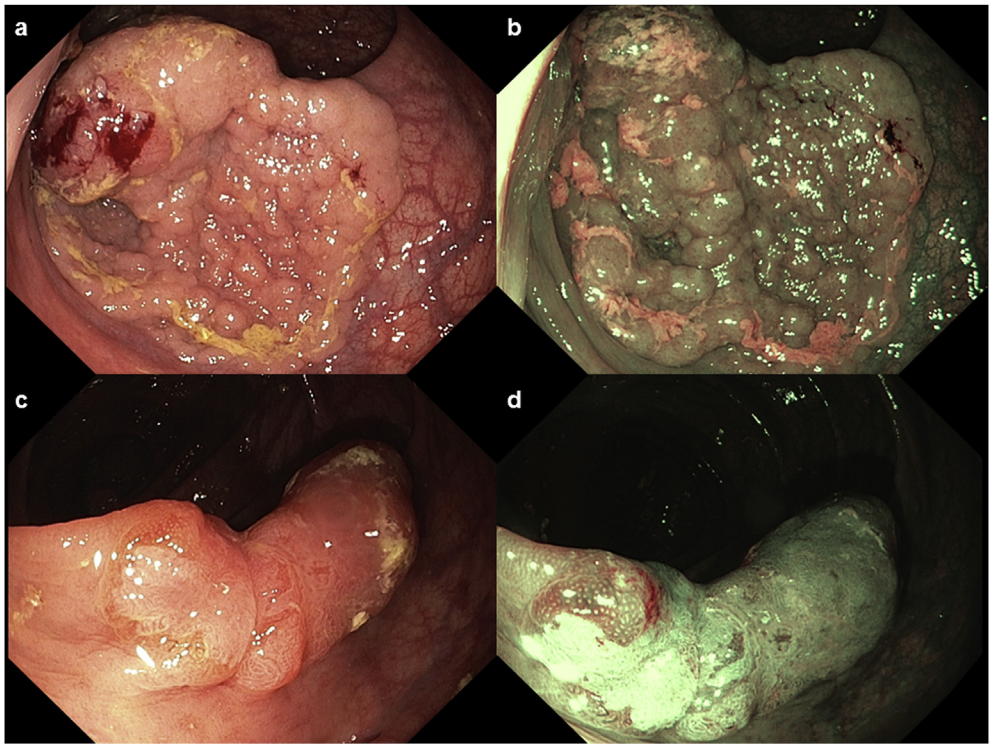

Fig. 3. Systematic approach to gastrointestinal lesion description. a and b: Located in sigmoid colon, size 50 mm, Paris 0-IIa + Is, granular LST with dominant nodule (left upper), Kudo IIIS/L, NICE 2. Treatment: piecemeal EMR. Histopathology: tubulovillous adenoma with low-grade dysplasia. c and d: Located in ascending colon, size 18 mm, Paris IIa–IIc, Kudo V, Nice 3, fold convergence. Treatment: referred for surgery. Histopathology: pT1sm3N0M0 adenocarcinoma.

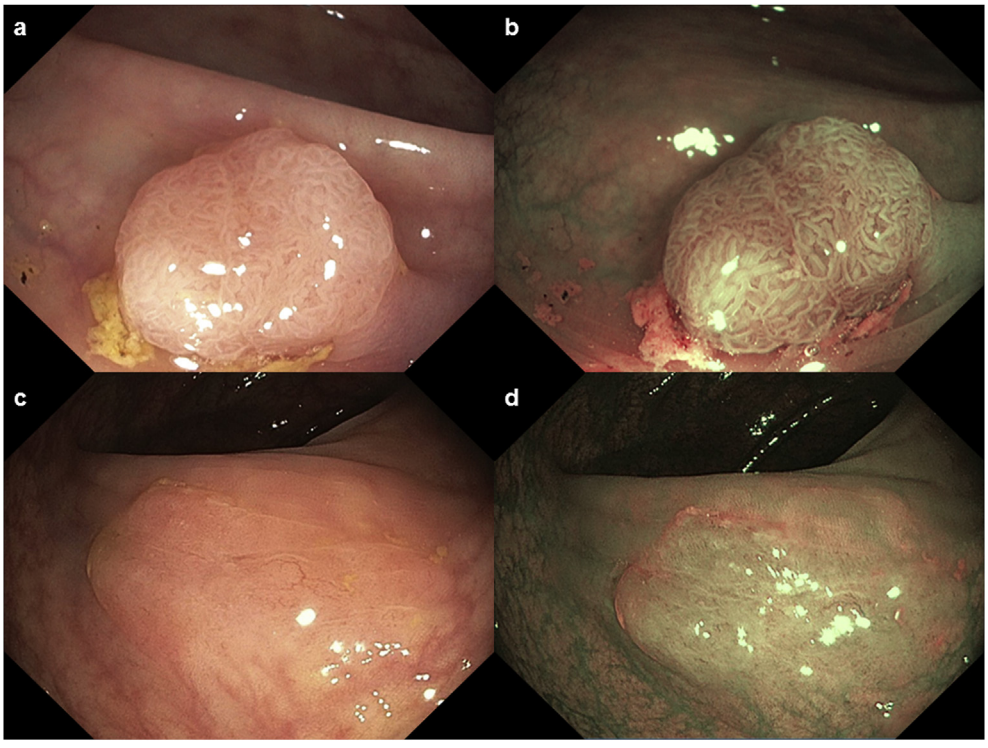

Fig. 4. Systematic approach to gastrointestinal lesion description. a and b: Located in descending colon, size 8 mm, Paris Is, Kudo IIIS/L, NICE 2. Treatment: hot polypectomy. Histopathology: tubular adenoma with low-grade dysplasia. c and d: Located in ascending colon, size 12 mm, Paris IIa, Kudo II, Nice 1, WASP features: clouded surface and indistinct borders. Treatment: EMR en-bloc. Histopathology: sessile serrated lesion without dysplasia.

adapted in clinical practice [26,69]. Lesions that exhibit a Kudo type V pit pattern or NICE type 3 should not be removed endoscopically in daily practice, but referred to an expert center for an optimal treatment decision.

Other morphological features associated with deep submucosal invasion

Other gross morphological features to identify lesions with an increased risk of deep invasive growth have been previously described in literature. Lesions exhibiting morphological features like sclerous wall change, fold convergence, surface redness, spontaneous bleeding, white spots and exudates are at risk for deep submucosal invasive growth [46,70,71]. In a systematic review, combinations of those gross morphological features resulted in a lower accuracy than optical diagnosis with NBI or magnification chromoendoscopy [68]. Therefore, we suggest that lesions exhibiting one of these gross morphological features warrant careful inspection of mucosal surface pattern with high-definition digital chromoendoscopy techniques as these may not be amenable to endoscopic resection.

Real-time decision making; what to do in clinical practice?

When encountering a lesion in the gastrointestinal tract, we propose a systematic approach to describe and report the lesion as a basis for determining whether it is suitable for endoscopic resection and the optimal resection technique (Figs. 3 and 4):

- consider the location of the lesion;
- determine the size in millimeters, preferably next to a reference of known size;
- assess the lesion for morphology according to the Paris and LST classification;
- determine the surface pattern with high-definition digital chromoendoscopy techniques by using the NICE and/or Kudo classification; and
- assess the lesion for other gross morphological features that may suggest deep submucosal invasion.

It is important to consider all these morphological factors together, as there is considerable interaction as was shown in the Australian ACE study: sessile lesions sized >20 mm with a combination of Paris IIa + IIc, non-granular LST and Kudo pit pattern type V harbored submucosal invasion in 56% [35]. Lesions that exhibit Paris IIc, non-granular LSTs, Kudo pit pattern type V, NICE type 3 or gross morphological features suggesting cancer (Fig. 2), are at increased risk for harboring cancer and should be carefully evaluated for treatment decision-making. When a decision is made to refer a patient for further treatment, tattoo-placement adjacent to the lesion and noted in the report ensures re-detection for both endoscopist and surgeon.

When a lesion is not exhibiting any of the morphological features summarized in Fig. 2, the lesion may be removed en-bloc or piecemeal to achieve a complete resection. In line with the most recent ESGE guideline, we recommend to refer patients with complex located lesions (ileocecal valve, peri-appendicular or peri-diverticular), lesions with a non-lifting sign without a morphological sign of submucosal invasion or lesions sized >40 mm to an expert setting (Fig. 2) [26,72].

Practice points

- Endoscopic identification of submucosal invasion of gastrointestinal lesions is important to determine optimal treatment strategies
- A systematic morphological assessment of location, size, Paris and LST classification, surface pattern and gross morphological features contributes to the identification of submucosal invasion
- Surface pattern characteristics of lesions should be assessed with high-definition digital chromoendoscopy techniques
- Both Paris classification and size are associated with a high interobserver variability, possibly limiting their use in clinical practice
- Lesions are preferably removed en-bloc. Piecemeal removal should only be attempted in absence of morphological signs of submucosal invasion. If there is suspicion of submucosal invasion and the lesion is possibly endoscopically removable, the lesion should be treated in an expert setting.

Research agenda

- Rigorous development and validation of novel training methods, tools or classifications to reduce inter-observer variability for determination of size and Paris classification of gastrointestinal lesions
- Formal comparison of different endoscopic classification systems for gastrointestinal lesions in daily clinical practice to determine the most optimal advanced endoscopic imaging classification system for assessing superficial and deep submucosal invasion
- Observational studies with training for community gastroenterologists to achieve high accuracy in endoscopic prediction of superficial and deep submucosal invasion

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