Best Practice & Research Clinical Gastroenterology 31 (2017) 359–367

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology

journal homepage: https://ees.elsevier.com/ybega/default.asp

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Morphological classifications of gastrointestinal lesions

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Keywords:
Gastrointestinal polyps
Morphology
Structured reporting
Cancer

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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http://dx.doi.org/10.1016/j.bpg.2017.05.005
1521-6918/

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