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Guidelines

Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection

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Suitable lesions for endoscopic treatment include not only early colorectal carcinomas but also several types of precarcinomatous adenomas. It is important to establish practical guidelines wherein preoperative diagnosis of colorectal neoplasia and selection of endoscopic treatment procedures are appropriately outlined and to ensure that actual endoscopic treatment is useful and safe in general hospitals when carried out in accordance with guidelines. In cooperation with the Japanese Society for Cancer of the Colon and Rectum, the Japanese Society of Coloproctology, and the Japanese Society of Gastroenterology, the Japan Gastroenterological Endoscopy Society compiled colorectal endoscopic submucosal dissection/endoscopic mucosal resection guidelines by using evidence-based methods in 2014. The first edition of these guidelines was published 5 years ago. Accordingly, we have published the second edition of these guidelines based on recent new knowledge and evidence.

Key words: colorectal tumor, early colorectal carcinoma, endoscopic mucosal resection, endoscopic submucosal dissection, guidelines

INTRODUCTION

AT PRESENT, VARIOUS techniques are available for endoscopic treatment of colorectal tumors. Basically, complete en bloc resection is indicated for early colorectal carcinoma regardless of tumor size. Although endoscopic submucosal dissection (ESD) has recently made it easier, carrying out colorectal ESD is still technically more difficult than upper gastrointestinal ESD, and it is essential to prevent complications such as perforation. In contrast, among epithelial colorectal tumors that can be treated by endoscopic treatment, there are numerous adenomatous lesions that may be regarded as precarcinomatous in addition to early carcinomas. Therefore, accurate and qualitative preoperative diagnosis of lesions and selection of appropriate treatment on the basis of precise diagnosis are essential.

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In 2014, the Guidelines Committee of the Japan Gastroenterological Endoscopy Society (JGES) drafted the first edition of the colorectal ESD/endoscopic mucosal resection (EMR) guidelines (hereinafter referred to as the Guidelines).[1] The first edition of these guidelines was published 5 years ago. Accordingly, JGES has published the second edition of these guidelines based on recent new knowledge and evidence in accordance with Procedures for the Evaluation, Selection, and Publication of Japanese Clinical Practice Guidelines in Medical Information Network Distribution Service (MINDS) 2014,[2] taking into account strength of recommendations and levels of evidence (Table 1). The revised guidelines also focused on diagnostic and therapeutic strategies and stipulations before, during, and after EMR and ESD and did not contain any specific information regarding procedures, types, and appropriate use of instruments, devices, and drugs. These guidelines describe in detail the differences between colorectal EMR and ESD, preoperative diagnosis, and perioperative care.

In the revised guidelines, systematic document retrieval was conducted by searching PubMed and Igaku Chuo Zasshi for articles published from 1985 to 2018. Manual

searches were carried out for insufficient or unsearchable documents. Members of the Guidelines Creation Committee set the strength of recommendations and levels of evidence in their responsible fields by using the MINDS Grade of Recommendations, as described earlier.[2] For created statements, members of the Guidelines Creation Committee voted by using the Delphi method, as reported previously.[1]

INDICATION FOR ENDOSCOPIC OR SURGICAL TREATMENT

Basic principles

IN CASES OF early diagnosis of colorectal carcinoma, patients are recommended to undergo endoscopic or surgical treatment. According to a previous study, with surgical treatment, 5-year survival rates of stage 1 colon cancer and rectal cancer were 94% and 95%, respectively.[3] According to the Multi-Institutional Registry of Large Bowel Cancer in Japan, 5-year survival rates after surgery in colon cancer and rectal cancer were 91.6% and 88.5%, respectively, for stage 0 and 90.7% and 89.4%, respectively, for stage 1. Moreover, 5-year survival rates after endoscopic resection were 100% for intramucosal cancer (Tis) and 96.0% for submucosal (SM) invasive cancer (T1).[4]

In cases where the risk exceeds the benefit of endoscopic treatment, such as when a patient's general condition is extremely poor, it is recommended to abandon treatment. In particular, application of endoscopic treatment in elderly patients must be cautiously considered. Many elderly patients have poor general condition and suffer from comorbidities.[5] Frequency of complications associated with endoscopic treatment is high in such patients.[6,7] In contrast, certain reports have indicated that endoscopic treatment can be safely carried out even in elderly patients.[8,9] For very elderly patients, endoscopic treatment should be carried out only when the expected advantage is likely to outweigh the risk of complications associated with resection, while also considering average life expectancy, comorbidities, and physical age of the patient.

When carrying out endoscopic treatment, a patient's comorbidities and medications must be thoroughly evaluated. In particular, hemorrhage may develop when a patient taking an antithrombotic agent (anticoagulant or antiplatelet) undergoes endoscopic treatment without discontinuing the drug, whereas a cerebrocardiovascular event may occur if a patient discontinues this medication. After evaluating both risks, a decision should be made regarding whether the patient should continue to take the medication. If drug discontinuation is recommended, optimal timing for drug discontinuation and resumption must be carefully evaluated.[10,11] The risk of thromboembolism differs depending on the status of the patient's underlying disease, and the type and time of placement of artificial valves or stents. The risk of hemorrhage differs depending on the type of endoscopic examination and treatment. Both ESD and EMR are considered to have a high risk of hemorrhage.

As a general rule, written informed consent (IC) for carrying out endoscopic treatment must be obtained from the patient. The IC form must contain following items: (i) name and condition of the patient's disease; (ii) reasons for recommending endoscopic treatment; (iii) actual details of the procedure to be carried out; (iv) expected outcomes; (v) predicted risks; (vi) alternative methods that could substitute endoscopic treatment and information on the comparison; and (vii) prognosis if the patient does not undergo endoscopic treatment. When it is difficult to sufficiently communicate with a patient, IC must be obtained from an appropriate representative. With regard to use of sedation during endoscopic treatment, it is advisable to obtain IC where the expected effect and risk of complications are fully explained in a written document.

Indication for endoscopic treatment

Noncarcinoma

Resection is recommended for adenomas ≥6 mm in size. In addition, resection is recommended for superficial depressed-type lesions (type 0–IIc) even when the lesion is ≤5 mm in size. Typical hyperplastic polyps ≤5 mm in size that are present in the distal colon may be left untreated (strength of recommendation: 1, level of evidence: C). Carcinoma rate of protruded-type and superficial elevated-type lesions that are ≤5 mm in size is low, and such lesions are extremely unlikely to become T1 (SM) carcinoma. However, the rate of SM invasion (i.e. the T1 [SM]

Table 1 Strength of recommendations and levels of evidence based on recent new knowledge and evidence in accordance with Procedures for the Evaluation, Selection, and Publication of Japanese Clinical Practice Guidelines in MINDS 2014

Strength of recommendations
1: Strongly recommend to carry out
2: Weakly recommend (suggest) to carry out
None: No definite recommendation can be made
Levels of evidence
A (strong): Strongly confident in the effect of estimate
B (moderate): Moderately confident in the effect of estimate
C (weak): Confidence in the effect of estimate is limited
D (very weak): Almost no confidence in the effect of estimate

MINDS, Medical Information Network Distribution Service.

carcinoma rate of lesions >6 mm) increases as the size of the lesion increases.[12–17] Although adenomas themselves are benign, their removal is expected to prevent development of colorectal carcinoma.[18,19] Despite an extensive search of available literature, we could find no clear evidence regarding the rate of development into carcinoma and prognosis of diminutive lesions ≤5 mm in size in cases where such lesions are left untreated. Certain studies have reported that colorectal adenomas ≤5 mm in size that had been followed for several years showed null or minimal changes.[20–22] A previous study reported that there was no significant difference in the 5-year cumulative incidence of advanced colorectal neoplasia (ACN) between patients with untreated diminutive adenomas and those with no adenomas and that no ACN developed from unresected adenomas.[23] Therefore, prompt treatment may not be required for protruded-type and superficial elevated-type adenomas ≤5 mm in size.[1] In contrast, superficial depressed-type lesions show a certain carcinoma rate and a certain rate of SM invasion even when their size is ≤5 mm[12,13,15,16] and, therefore, these should be removed. Most colorectal neoplasms are adenomas, and these adenomas can be cured by using EMR or piecemeal EMR techniques.[24,25] For certain neoplasms, carrying out endoscopic treatment is technically challenging depending on the site or size of the lesion.

According to genetic–molecular pathological analyses, certain colorectal carcinomas are assumed to develop from serrated lesions through the so-called serrated pathway. However, the natural history and carcinoma rate of serrated lesions have not been sufficiently elucidated. Risk of colorectal carcinoma is reported to be high in patients with sessile serrated adenoma/polyp (SSA/P), particularly in those patients with serrated polyposis syndrome.[26–32] However, data on how often and how fast carcinoma development occurs within SSA/P itself are insufficient.[33–37] Reported cases of serrated lesions harboring carcinoma were mostly ≥10 mm but rarely 5–10 mm in diameter. Large or dysplastic SSA/P has the potential of developing into a carcinoma. In contrast, the possibility of carcinoma development is considered extremely low for typical hyperplastic polyps ≤5 mm in size present in the distal colon or rectum.[38] According to a previous study,[39] Tis and SM (T1) cancer accounted for only 0.7% and 0.2%, respectively, of all SSA/P, and the average size of these lesions was 18 mm. In the West, the guidelines recommend that any serrated lesion proximal to the splenic flexure should be removed,[1] whereas typical hyperplastic lesions in the rectosigmoid can be left unresected.[40] However, available evidence to support this policy may not be adequate. In Japan, management strategies for serrated lesions vary across different institutes. Evidence-based clinical practice guidelines for management of colorectal polyps in Japan[41] do not present any statement on this topic.

Western guidelines recommend that any neoplastic polyp detected should be resected. The aim of this policy is to extend the period before the next surveillance colonoscopy, which can be a substantial economic burden for patients in localities where such procedures are expensive. In Japan, indication for resection is determined based on characterization of the polyp through careful and meticulous observation by using image-enhanced colonoscopy, including chromoendoscopy and magnification.

Carcinoma

Among early colorectal carcinomas (Tis/T1), lesions with limited possibility of lymph node metastasis that seem resectable en bloc on the basis of size and location are recommended for endoscopic treatment because such cases are expected to be curable. Obvious clinical T1b carcinomas are recommended to be treated surgically (strength of recommendation: 1, level of evidence: C).

Among endoscopic treatments, ESD is the most suitable method for en bloc resection, particularly for large lesions.[42–48] Piecemeal EMR may make it difficult to establish pathological diagnosis of the invasion depth and to determine a free resection margin. Number of resected pieces must be minimized, and the region suspected to contain a carcinoma should not be sectioned. Local recurrence rate increases with larger tumor size and greater number of resected pieces.[49–53] When carrying out piecemeal EMR, magnifying endoscopic observation, which is the best way to identify the carcinomatous part of a lesion, should be done before treatment, and the carcinomatous area should not be sectioned. Otherwise, it would be difficult to evaluate invasion depth or vessel invasion, and additional treatments such as lymph node dissection might not be carried out even when it is necessary in cases of SM invasive carcinoma.

Laterally spreading tumors (LST) are classified into granular type (LST-G) and nongranular type (LST-NG). In LST-NG, the pseudo-depressed type (PD), which is expressed as IIc + IIa or IIa + IIc according to the Japanese Classification of Colorectal Carcinoma,[54] is associated with multifocal invasion, the foci of which are often difficult to predict. In addition, LST-NG (PD) is frequently associated with fibrosis. Therefore, in several cases, EMR is not suitable for LST-NG (PD).[55] Considering the high possibility of deep SM invasion in LST-NG (PD), whether the lesion is indicated for surgical operation or for endoscopic treatment should be cautiously considered. To determine the indication for ESD or EMR for LST, overall judgment

based on the subclassification of LST (Fig. 1) and the pit pattern diagnosis by using magnifying observation is useful.[56] Details of evaluating lesions for the ESD technique are presented in Table 2.[45,46,57–59]

PREOPERATIVE DIAGNOSIS

Distinction between adenoma and adenocarcinoma

BEFORE CARRYING OUT colorectal ESD or EMR, it is important to distinguish between adenomas and adenocarcinomas in order to determine whether the lesion is benign or malignant and to characterize marginal demarcation of the lesion. In the large intestine, adenoma and "carcinoma in/with adenoma" lesions are often detected in addition to early carcinomas without adenoma. Therefore, not only the malignancy of an entire lesion but also carcinomatous and adenomatous parts of the lesion must be correctly assessed and distinguished. Consequently, therapeutic strategies such as use of ESD or EMR, selection of

Table 2 Indications for endoscopic submucosal dissection of colorectal tumors

Lesions for which endoscopic en bloc resection is required
1) Lesions for which en bloc resection with snare EMR is difficult to apply
LST-NG, particularly LST-NG (PD)
Lesions showing a VI-type pit pattern
Carcinoma with shallow T1 (SM) invasion
Large depressed-type tumors
Large protruded-type lesions suspected to be carcinoma[†]
2) Mucosal tumors with submucosal fibrosis[‡]
3) Sporadic tumors in conditions of chronic inflammation such as ulcerative colitis
4) Local residual or recurrent early carcinomas after endoscopic resection

EMR, endoscopic mucosal resection; LST-G, laterally spreading tumor granular type; LST-NG, laterally spreading tumor nongranular type; PD, pseudo-depressed; SM, submucosal.
[†]Including LST-G, nodular mixed type.
[‡]As a result of a previous biopsy or prolapse caused by peristalsis of the intestine.

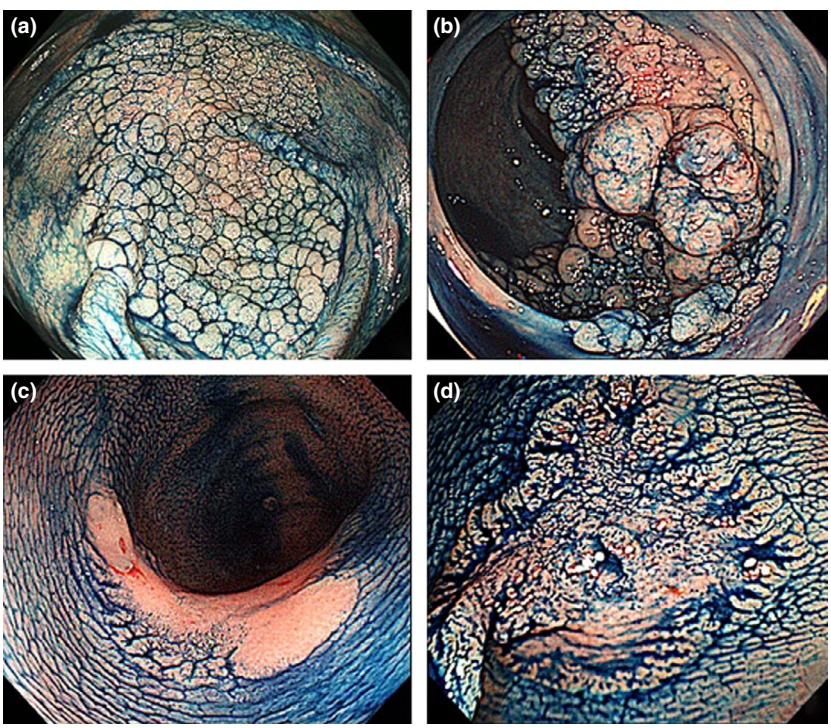

Figure 1 Subtypes of laterally spreading tumors (LST; classification should be done on the basis of images obtained by using indigo carmine dye spraying). LST-G, laterally spreading tumor granular type; LST-NG, laterally spreading tumor nongranular type. (a) Homogeneous type LST-G (Homo); (b) nodular mixed-type LST-G (Mix); (c) flat-elevated-type LST-NG (F); and (d) pseudo-depressed type LST-NG (PD).

piecemeal EMR, and a deliberately planned sectioning line can be determined.[60]

Distinction between adenoma and adenocarcinoma with high accuracy can be achieved with use of image-enhanced endoscopy and magnifying observation (strength of recommendation: 2, level of evidence: A). For distinction between adenomas and adenocarcinomas, lesion color, surface unevenness, presence of depression, and fold convergence must be confirmed by ordinary observation and chromoendoscopic observation. At present, magnifying observation (pit pattern diagnosis) using dye spraying (indigo carmine, crystal violet, and so on) and image-enhancement technology (e.g. narrow band imaging [NBI] and blue laser imaging [BLI]) could be used for diagnosing lesions on the basis of detailed visualization of fine surface structures (surface pattern) and microvessels.[61–63] According to previous studies, the diagnostic accuracy rate of discriminating neoplastic from nonneoplastic lesions is approximately 80% for standard observation, including magnifying chromoendoscopic observation, 96%–98% for pit-pattern observation, and 95% for magnifying observation with use of NBI and BLI.[64–70] Accuracy rate of discrimination between adenomas and carcinomas was 70%–90% for pit-pattern observation, and a similar rate has been reported for NBI. Thus, distinction between adenomas and adenocarcinomas with high accuracy can be achieved with magnifying endoscopic observation.[71–75]

Although various classifications have been proposed for diagnosis using NBI, internationally, it is unified with the NICE classification (NBI International Colorectal Endoscopic classification)[76] without/with magnification and the JNET classification (Japan NBI Expert Team classification) by magnification.[77]

More recently, the introduction of endocytoscopy and confocal laser endomicroscopy has made it possible to observe cellular levels *in vivo*. Although these methods have shown extremely high diagnostic accuracy over magnifying endoscopes,[78,79] use of such methods is not yet common.

Thus, the evidence that endoscopic diagnosis has reached a level close to histopathological diagnosis is well demonstrated by advances in endoscopic equipment.

However, the penetration rate of these devices is not sufficient, and the problem of maintenance in each facility remains; hence, the "strength of recommendation" was set at level 2.

In contrast, SSA/P and TSA, which are included in serrated lesions regarded as nonneoplastic lesions in the past, are noted as precursor lesions of cancer.[80] Reportedly, image enhancement/magnifying endoscopic diagnosis is also useful in qualitative diagnosis of such lesions, including carcinoma cases.[81–87] In addition, biopsy should not be done in principle for qualitative diagnosis (strength of recommendation: 2, level of evidence: C). In cases of superficial-type lesions, because biopsy as a preoperative diagnosis may cause fibrosis in the SM layer and lead to a positive nonlifting sign, subsequent endoscopic treatment will be difficult.[81] For large lesions such as LST-G,[54] which, in several cases are "carcinoma in adenoma", a simple biopsy may not show an accurate yield as a qualitative diagnosis. Therefore, a diagnosis based on image enhancement/magnifying endoscopic observation as an optical biopsy (histological diagnosis by endoscopic imaging without forceps biopsy) is more effective.

Diagnosis of invasion depth

For early colorectal carcinoma, it is necessary to estimate the degree of SM invasion before carrying out endoscopic treatment (strength of recommendation: 1, level of evidence: A). Risks of vascular invasion and lymph node metastasis differ according to SM invasion depth of a carcinoma. For deep invasive T1 (SM) carcinoma, the risk of incomplete resection is high in endoscopic treatment. Therefore, the degree of SM invasion must be estimated before carrying out endoscopic treatment. Furthermore, to conduct accurate pathological evaluation of endoscopically resected specimens, it is important to indicate the section with SM invasion in the entire lesion.[60]

When diagnosing invasion depth, if a deep depression, expansive appearance, SM tumor-like margin, or defective extension is detected during ordinary or chromoendoscopic observation, deep SM invasion may be considered; the accuracy rate of deep SM invasion is 70–80%.[88,89] In pit-pattern diagnosis with dye-spraying magnifying endoscopic observation, an accuracy rate of approximately 90% can be obtained if the VN-type pit pattern is observed. The accuracy rate of protruded-type lesions tends to be slightly lower than that of superficial-type lesions.[90–92]

Furthermore, equivalent diagnosis is possible with the NICE classification[93] and the JNET classification[94] by using NBI.

The accuracy rate is approximately 80% when ultrasonography is used; however, visualization capacity is affected by the condition and morphology of a lesion.[95–99] These diagnostic methods have certain advantages and disadvantages. As diagnostic accuracy differs according to the macroscopic type and growth type of the lesion, appropriate diagnostic methods should be combined as the situation requires.[100]

TECHNIQUES

Definition of ESD and EMR

IN EMR, [101,102] a normal saline solution or a sodium hyaluronate solution[103–105] is locally injected into the submucosa of a superficial-type tumor through the injection needle. The lesion is strangled with a snare and then resected by applying high-frequency current. Although polyp resection in cold polypectomy is carried out without applying high-frequency current, high-frequency current is essential in EMR and is fundamentally applied. In piecemeal EMR, a large nodule or carcinomatous region is first cut into a large piece to accurately carry out histological diagnosis, and the residual flat part is then deliberately cut into pieces; this is also known as planned piecemeal EMR. A new technique called "underwater EMR" has been developed in the USA, and it is applied for small colorectal adenomas even in Japan. This underwater EMR is a technique to snare the lesion under water without any liquid injection into the SM layer; therefore, it has not been categorized as EMR in these guidelines.[106,107]

In ESD, a normal saline solution or a sodium hyaluronate solution is locally injected into the submucosa of a tumor through the injection needle. The circumference of the lesion is then incised using a needle-type knife for ESD with electrical cutting current produced by the equipment, and the SM layer is then dissected. This technique can resect the lesion in one piece regardless of its size.[45,47,108–111]

In the Guidelines, specific terminology is used to distinguish several forms of ESD, as follows. A technique wherein dissection of the SM layer is completed without using a snare is defined as "actual (narrowly defined) ESD".[112,113] Similarly, a technique wherein snaring is carried out without dissecting the SM layer after incising the circumference of the lesion alone, by using a knife for ESD or the tip of a snare, is defined as "precutting EMR".[114] Finally, a technique wherein the SM layer is dissected and snaring is carried out after the ESD procedure (mucosal incision + SM dissection), by using a knife for ESD or the tip of a snare, is defined as "hybrid ESD".[112,113,115] Other terminologies for precutting EMR[114] and hybrid ESD are reported in the literature, but the Guidelines use the terms defined above.

Choosing between ESD and EMR

En bloc resection is desirable as an endoscopic treatment for early colorectal carcinomas (strength of recommendation: 1, level of evidence: B). However, piecemeal EMR is permissible for certain adenomas and "carcinoma in adenoma" lesions when appropriately carried out. When performing piecemeal EMR, magnifying endoscopic observation should be cautiously carried out before treatment, and the carcinomatous area should never be cut into pieces. The reason for this restriction is that if SM invasive carcinoma is cut into pieces, pathological diagnosis for the invasion depth and lymph-vascular invasion would be difficult, and necessary additional treatment might not be given.[22,47,55,116,117] Previous reports have shown that when piecemeal EMR is carried out, magnifying endoscopic observation of the lesion margin and ulcer base after resection is useful to decrease the local residual/recurrence rate.[118] To confirm local residual/recurrence, follow-up colonoscopy should be done approximately 6 months after treatment.[49,119–121]

Frequency of T1 (SM) carcinomas increases as tumor size increases. With multi-piecemeal resection, which makes pathological reconstruction of a tumor challenging, histological evaluation is also difficult and the local residual/recurrence rate is higher.[49,115,119,120] For large lesions with a size greater than half of the circumference of the colorectal lumen, piecemeal EMR should be avoided, and ESD should be carried out by a skilled endoscopist. Only when ESD is not possible, surgery is considered as an alternative treatment.[46,109,110]

Following development of requisite devices and establishment of appropriate methods, colorectal ESD can be safely and accurately carried out by experts. However, when performing ESD, it is important to prepare various devices (ESD knives, devices, distal attachments, local injection agents such as sodium hyaluronate,[103–105] a carbon dioxide insufflator,[108] and endoscopic clips) to prevent and treat adverse events such as perforation and to ensure that there are appropriate facilities for hospitalization and surgical treatment.

Endoscopic treatment for lesions positive for the nonlifting sign

Although a majority of such lesions are T1 carcinomas, a lesion showing a positive nonlifting sign can potentially be a mucosal tumor (adenoma or mucosal carcinoma). Therefore, if a lesion is endoscopically judged as a mucosal tumor, ESD/EMR is appropriate (strength of recommendation: 2, level of evidence: B).

For mucosal lesions that are nonlifting sign positive[122–124] and residual/recurrence lesions, ESD can resect those lesions wherein EMR is generally difficult and for which *en bloc* resection is desirable (in particular, lesions suspected to be early carcinomas and LST-NG). However, ESD must be cautiously carried out while checking for perforation.[45,55,125–127]

The nonlifting sign[122,123] is a sign that helps diagnose the depth of carcinoma invasion and is often used in clinical practice. However, a multicenter study[124] showed that diagnostic sensitivity of conventional endoscopic observation for deep SM invasive carcinoma was superior to that of a nonlifting sign (84.6% *vs* 61.5%). Colorectal tumors occasionally show a positive nonlifting sign as a result of peristaltic motion or fibrosis caused by biopsy, although such lesions are usually of the mucosal type.[122,123] Therefore, preoperative endoscopic diagnosis should be carefully made by magnifying endoscopic observation before endoscopic treatment for neoplastic lesions. Once the targeted lesion is diagnosed as carcinoma, the invasion depth should be diagnosed by magnifying endoscopy, and biopsy should be avoided.

Endoscopists who carry out colorectal ESD should be registered with the Japan Gastroenterological Society (JGES) or must have skills similar to those of registered endoscopists in Japan. Familiarity with esophageal and gastric ESD alone may be insufficient. Minimum requirements for endoscopists are as follows: (i) have sufficient understanding of anatomical features of the large intestine; (ii) have the skill to perform an insertion technique by which the colorectal endoscope could be smoothly and accurately advanced to the cecum in the shortest distance possible; and (iii) have familiarity with basic techniques of polypectomy, EMR, hemostasis, and clip suture. Experience with gastric ESD is helpful in preparation for colorectal ESD. If the experience of the endoscopist is limited to colorectal examination, colorectal ESD should be carried out only after sufficient training in ESD by using living or isolated porcine stomach or colon.[128–130]

COMPLICATIONS DURING PROCEDURES

PRIMARY ACCIDENTAL COMPLICATIONS during colonoscopic treatment are perforation and bleeding. Perforation is a condition wherein the abdominal cavity is visible from the colorectal lumen because of mural tissue defects. The presence of free air is not always detected on X-ray examination. In contrast, the condition wherein the tissue defect reaches other parenchymal organs is defined as penetration. Various definitions have been proposed for bleeding, such as a decrease in hemoglobin by >2 mg/dL or the requirement for blood transfusion. However, these definitions have not been established on the basis of solid evidence. With regard to frequency of these accidental complications, perforation rates during endoscopic resection are reported to be 0%, 0–0.8% and 2.0–10.7% for polypectomy, EMR, and ESD, respectively, according to recent publications (Table 3).[48,111,131–134]

Table 3 Perforation rate during procedure in accordance with resection technique

Perforation rate			Author
Polypectomy	EMR	ESD	
—	0%	10.7%	Kobayashi *et al*. (2012)[48]
—	0.8%	2.0%	Nakajima *et al*. (2013)[111]
0%	0.78%	—	Wada *et al*. (2015)[131]
—	—	5.5%	Fujishiro *et al*. (2007)[132]
—	—	8.2%	Isomoto *et al*. (2009)[133]

—, no data.
EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

Management of perforation

As the colonic wall is thinner than that of the stomach, risk of perforation during the procedure is higher in the colon than in the stomach. Before the procedure, sufficient bowel preparation is required to prepare for the possibility of perforation. During the procedure, it is essential to ensure good maneuverability of the scope. It is important to select a scope according to the location and morphology of the tumor, and it is necessary to use appropriate devices, local injection agents, and a carbon dioxide insufflator for a successful procedure.[108,135] When perforation occurs during the procedure, clipping should be carried out as far as possible, regardless of the location (strength of recommendation: 1, level of evidence: C). Clipping should be done after creating sufficient space to apply endoclips in case of ESD as applied clips often disturb subsequent SM dissection. When closure of the perforation is complete, surgical rescue can usually be avoided by giving i.v. antibiotics and fasting.[132,136,137] The presence of free air within the abdominal cavity after perforation on computed tomography (CT) evaluation cannot be used to guide the decision for emergency surgery.[137] It is necessary to carefully decide the timing of emergency surgery by checking abdominal symptoms and laboratory data in cooperation with surgeons. Nevertheless, in cases of incomplete closure of the perforation, emergency surgery should be carried out as soon as possible as the risk of pan-peritonitis is extremely high in such situations.

In cases of rectal lesion below the peritoneal reflection, perforation into the abdominal cavity does not occur as a result of anatomical features; however, penetration into the retroperitoneum occurs and, consequently, mediastinal emphysema or subcutaneous emphysema may occur.[138]

Management of bleeding

For bleeding associated with endoscopic resection, clipping or coagulation is appropriate. In cases of minor bleeding

from a small vessel, contact coagulation with the tip of a snare during EMR or with the tip of a knife during ESD or coagulation with hemostatic forceps is usually used for hemostasis. In cases of severe bleeding from a large vessel or artery, hemostatic forceps are indispensable. To avoid delayed perforation caused by thermal damage, the bleeding point should be grasped precisely with hemostatic forceps, and application of electrocoagulation should be minimized. In general, severe bleeding that requires clipping seldom occurs in the colon; however, clipping is easy and effective after complete resection of the lesion with EMR. Meanwhile, clipping should be carefully done during ESD as applied clips can disturb the subsequent procedure.

PERIOPERATIVE CARE BEFORE AND AFTER ENDOSCOPIC TREATMENT

DURING PERIOPERATIVE CARE after endoscopic treatment, attention should be paid to delayed perforation and delayed bleeding, and patients should be hospitalized if necessary (strength of recommendation: 2, level of evidence: C). Perioperative care should be considered during the clinical practice of ESD/EMR, including the hospitalization period.[139] For patients using antithrombotic drugs who will undergo ESD/EMR, the reader is referred to the "Guidelines for Gastroenterological Endoscopy in Patients Undergoing Antithrombotic Treatment" published by JGES[10] as well as the revised guidelines.[11]

Antithrombotic drugs

The aforementioned guidelines propose a strategy wherein patients who undergo ESD/EMR are divided into high- and low-risk groups according to the predicted risk of thromboembolism. The way in which antithrombotic drugs are handled in pre-/post-ESD/EMR procedures is dependent on the risk of thromboembolism in patients, and published JGES guidelines should be referred to for further details.

1. Endoscopic submucosal dissection/EMR procedures planned in patients taking antithrombotics (aspirin, thienopyridine) should be carefully carried out, and procedures should be postponed until antithrombotics can be withdrawn or are recommended to be replaced with aspirin or cilostazol.
2. Endoscopic mucosal resection/ESD procedures planned in patients taking warfarin in combination with antiplatelet drugs can be carried out with warfarin ongoing if prothrombin time–international normalized ratio (PT-INR) is within the control level or warfarin can be temporarily replaced with direct oral anticoagulants (DOAC).
3. Direct oral anticoagulants can be stopped on the day of EMR/ESD because of its extremely short acting time.
4. EMR/ESD procedures planned in patients taking DOAC and antiplatelet drugs can be performed with DOAC off on the day of EMR/ESD, and the antiplatelet drug can be replaced with aspirin or cilostazol.

After withdrawal of an antithrombotic drug, the drug can be given again when hemostasis is endoscopically confirmed. Careful observation is advised against post-procedure hemorrhage after antithrombotic drugs are resumed.

It is clinically important to consider the risk and benefit of stopping or continuing antithrombotic drugs during EMR/ESD. Compared with gastric ESD, the risk of delayed bleeding is lower and not fatal in colorectal EMR/ESD.

Bowel preparation

After confirming no stenosis of the digestive tract, a diet preparation for colonoscopy (or food in accordance with the diet) and a laxative are given at bedtime on the night before the procedure. On the day of colonoscopy, 2–3 L of an intestinal lavage solution is given. In cases where pretreatment is incomplete, additional intestinal lavage or split dose preparation (2 L on the day before and 1 L on the same day) could be considered.

With regard to premedication and sedation, as intestinal peristalsis may hinder the treatment, if possible, a spasmolytic (scopolamine Buscopan; Boehringer Ingelheim, Tokyo, Japan) is (i.v. or i.m.) injected after confirming that no contraindication (glaucoma, prostatic hypertrophy, and arrhythmia) is present. Use of a sedative/analgesic is determined according to the endoscopist's judgment and the patient's wishes. Although infrequent, careful attention should be paid to any occurrence of anaphylactic shock. However, excessive sedation should be avoided in colorectal ESD/EMR because position changes are often required. Abdominal fullness can be reduced through carbon dioxide insufflation, thereby decreasing the amount of sedatives required.[108,135]

Intraoperative management

Oxygen concentration, electrocardiogram, and blood pressure should be monitored during the procedure when sedation is necessary and a procedure of long duration is planned.

Postoperative management

In the Japanese situation, EMR for lesions <2 cm in size can be carried out for outpatients. In contrast, EMR and ESD for lesions >2 cm in size should be done after the patient is hospitalized. However, no recommendations are provided in these guidelines for the length of hospitalization and the timing of oral ingestion after endoscopic procedures. In addition, EMR and ESD are frequently done during the day in Western countries because of insurance difference and high hospitalization costs. One report regarding ESD showed that no adverse events occurred in a clinical pathway where the length of hospitalization was 4 nights and 5 days with oral ingestion starting 2 days after ESD.[139] A meal is given after confirming the absence of inflammatory findings, such as level of serum C-reactive protein, abdominal pain, and fever, while checking for delayed perforation and delayed bleeding. Both the length of hospitalization and the fasting period should be considered with regard to each specific situation.

Post-polypectomy electrocoagulation syndrome

Even in cases where no perforation has developed, abdominal pain or fever may occur if the muscular layer is ruptured or thermally denatured. Pain and fever may be caused by inflammation of the peritoneum, which occasionally occurs after electrocoagulation, even when no subsequent perforation occurs.[140] Although for most patients conservative treatment can generally be carried out, it is important to adopt careful measures such as prolongation of the fasting period while considering the possibility of delayed perforation.

Delayed perforation

Delayed perforation is intestinal perforation that develops a certain period of time after ESD/EMR (i.e. intestinal perforation that is detected after the scope has been withdrawn following completion of ESD/EMR during which perforation did not occur). Delayed perforation is diagnosed on the basis of abdominal pain, abdominal findings, presence of fever, and inflammatory response. Most cases of delayed perforation occur within 14 h after ESD/EMR. However, approximately one-third of delayed perforation cases are confirmed 24 h after treatment. Free air, which cannot be detected by simple X-ray imaging, is occasionally detected on abdominal CT. Therefore, in cases where delayed perforation is suspected, abdominal CT should be carried out. Surgeons must be called for emergency surgery, which is essential in cases of delayed perforation. The incidence of delayed perforation is 0% in EMR (no data have been reported) and 0.1–0.4% in ESD (indicating that delayed perforation seldom occurs).[45,111,141]

Significant delayed bleeding

Delayed bleeding is defined as a decrease in hemoglobin by >2 g/dL or confirmation of marked hemorrhage a certain period of time after endoscopic treatment.[142] Significant delayed bleeding does not include small amounts of bleeding such as presence of trace amounts of blood in the stool. The incidence of delayed bleeding is reported to be 1.4–1.7% in EMR[111,120] and 1.5–2.8% in ESD.[45,111,120,141] Delayed bleeding is primarily observed during the period between 2 and 7 days after ESD/EMR, and hemorrhage observed within 10 days after ESD/EMR may be considered delayed bleeding. Effect of application of a prophylactic clip on delayed bleeding has been discussed previously. A study reported that prophylactic clip application was effective for lesions >20 mm in size.[143] A recent US multicenter randomized trial, however, found that prophylactic placement of hemoclips after removal of large colon polyps does not influence the rate of important post-endoscopic resection bleeding.[144]

The effectiveness of prophylactic clip application for high-risk lesions must be further evaluated through high-quality prospective studies.

A previous study reported that delayed bleeding rate after polypectomy was significantly higher in the patient group taking anticoagulant drugs than in the patient group not taking them (2.6% *vs* 0.2% [$P = 0.005$]).[145]

Fournier's syndrome (fulminant necrotizing fasciitis)

In cases where the rectum is below the peritoneal reflection, perforation into the abdominal cavity does not occur because of anatomical features; however, penetration into the retroperitoneum occurs and, consequently, mediastinal emphysema or subcutaneous emphysema may occur.[138] Moreover, the possibility of fulminant necrotizing fasciitis (Fournier's syndrome) cannot be dismissed, although it is extremely rare, and no study has reported its development after endoscopic resection.[146] However, when fulminant necrotizing fasciitis develops, it causes septicemia and disseminated intravascular coagulation, and the associated mortality is reported to be 20–40%. Therefore, broad-spectrum antibiotics and immediate surgical treatment are required.[147]

ASSESSMENT OF CURABILITY

OBSERVATION WITH MAGNIFYING endoscopy is the most important method for evaluating local recurrence. Curability is evaluated based on the tumor margin of the resected specimen and the risk factors for lymph node/distant metastasis are considered for final diagnosis. In addition to the final diagnosis, confirming the pathological diagnosis of the resected specimen is also crucial. Because if treated inappropriately, histopathological evaluation such as lympho-vascular invasion and the distance of the depth invasion into the submucosal layer will be impossible to diagnose correctly, It means that there is a risk of being left without the additional resection in the sense of preventing from the residual recurrence and lymph node metastasis.

Adenoma

Adenomas (tubular, tubulovillous, villous, and serrated adenomas) are defined as benign tumors. Therefore, complete resection of these is possible unless there are residual lesions at the incised margin.[148–151]

Tis (M) carcinoma

With regard to colorectal tumors, Tis (M) carcinomas generally do not metastasize to lymph nodes or other organs. These lesions can be radically cured by endoscopic *en bloc* resection without neoplastic lesions at the incised margin. However, in cases with positive lateral tumor margins or piecemeal resection, local recurrence has been reported (Table 4).[49,146,148] Such cases are evaluated as local curative only endoscopically.

T1 (SM) carcinoma

When pT1 (SM) carcinoma is detected in pathological examination after endoscopic treatment, the subsequent therapeutic course should be determined in accordance with the 2019 Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines for the Treatment of Colorectal Cancer.[60] Additional surgical operation should be carried out for deep tumor margin-positive lesions as a result of incomplete endoscopic resection (highly recommended). In the case of complete endoscopic resection, pT1 (SM) carcinomas can be judged to have been radically cured when all of the following conditions are satisfied on histological analysis: (i) vertical tumor margin-negative (histological complete resection); (ii) papillary adenocarcinoma or tubular adenocarcinoma; (iii) SM invasion depth <1000 μm; (iv) no vascular invasion; and (v) tumor budding grade 1 (low grade). In these cases, careful observation is advised because the incidence of recurrence is extremely rare (strength of recommendation: 2, level of evidence: B).

If even one of these five conditions is encountered, the estimated rate of lymph node metastasis of the lesion and the background of the patient (i.e. age, coexisting disease, physical activity, intention, and quality of life after surgery that includes factors such as construction of an artificial anus) are comprehensively evaluated, and the indication for additional surgical resection is considered (low recommendation). Additional surgical resection is never forcibly carried out. These conditions are comprehensively evaluated, and a course involving either follow up or additional resection is selected accordingly.[152]

Table 4 Local recurrence rate between *en bloc* and piecemeal resection

Resection method		Author
En bloc	Piecemeal	
2.7%	20.1%	Saito *et al.* (2010)[47]
0–3%	10–23%	Hotta *et al.* (2010)[49]
—	19%	Sakamoto *et al.* (2012)[50]
1.4%	6.8%	Oka *et al.* (2015)[53]
0.7%	23.5%	Hotta *et al.* (2009)[119]
1.2%	15.4%	Tajika *et al.* (2011)[148]

—, no data.

Additional resection for T1 carcinoma

According to the study "The stratification of risk factors for the metastasis of pT1b SM cancer (SM invasion more than 1000 μm)" by Japanese Society for Cancer of the Colon and Rectum (JSCCR), the incidence of lymph node metastasis was 1.4% in cases wherein only SM invasion depth did not satisfy the criteria for radical cure and where no other risk factors for metastasis were observed.[153] In addition, studies have reported this incidence to range from 1% to 2% in similar situations.[154,155] In contrast, even if surgery was carried out at first, the incidence of metastatic recurrence was reported as 1.5% for colon and 4.2% for rectum.[156] The safety of surgery for colorectal cancers is considered extremely high; however, there were no deaths as a result of resection for colorectal cancers according to the report from the database of the Japanese Society of Gastroenterological Surgery[157] in 2009. Moreover, in other similar multicenter studies, this incidence was 2.3%[158] for right hemicolectomy and 0.9%[159] for low anterior resection. Based on the aforementioned findings, we must carefully consider patient background, pathological findings, and the advantage of additional resection for cases with a low risk of

recurrence as well as to decide treatment strategies for such patients.[160]

POSTOPERATIVE FOLLOW UP

THE AIM OF follow up after colorectal ESD/EMR is early detection of local residual/recurrence, metastasis, and metachronous[2] lesions.[161,162] Certain studies have reported that endoscopic treatment for colorectal tumors decreased the incidence of colorectal carcinoma and the risk of mortality.[163,164] Surveillance after surgical resection for colorectal carcinoma was reported to improve prognosis.[165] Nevertheless, there is no evidence-based consensus on actual follow-up methods after endoscopic treatment in Japan. The follow-up plan should be established with regard to therapeutic techniques such as *en bloc* resection and piecemeal resection, curability evaluation based on pathological examination of resected specimens, risk factors for multiple lesions and carcinomas, and underlying disease. In essence, the plan must give importance to the background of each patient.

Local residual/recurrence

For early detection of local residual/recurrence, periodic observation with colonoscopy is desirable, and endoscopic measures are applicable to several early detection cases. In adenoma or pTis (M) carcinomas, when piecemeal resection is used or the tumor margin after resection is unclear and curability cannot be accurately evaluated, colonoscopy should be carried out approximately 6 months after endoscopic treatment (strength of recommendation: 2, level of evidence: C). Compared with complete *en bloc* resection, histological evaluation is more challenging and the local residual/recurrence rate is higher with piecemeal resection.[166] Moreover, piecemeal resection is an independent risk factor for local recurrence, even after ESD is carried out for tumors >20 mm (Tables 4 and 5).[53] Recurrence rates were reported to be 18.4%, 23.1%, and 30.7% at 6, 12, and 24 months after piecemeal resection, respectively.[119] When the horizontal tumor margin is difficult to evaluate or when piecemeal resection is carried out, colonoscopy is recommended within 6–12 months.[59,156]

In the case of endoscopic treatment, recurrence or metastasis of pT1 (SM) carcinomas is reported to occur mainly within 3–5 years (Table 6).[167–170] One of these reports showed that among patients in whom no additional surgery was done who developed recurrent cancer, 41.7% died as a result of recurrent cancer.[170] Recurrence or metastasis of pT1 (SM) carcinomas occurs even in cases where surgical resection including lymph node dissection has been carried out. Furthermore, the recurrence rate in the rectum (4.2–4.5%) is higher than that in the colon (1.5–1.9%).[156,171] In particular, the rectum should be carefully observed. Reportedly, there was no difference in metastasis and recurrence rates between the group who had surgery from the beginning and the group who had surgery after endoscopic resection for pT1 (SM) carcinoma.[169,172] Hence, endoscopic resection did not worsen clinical outcomes of patients who required additional surgical resection.

Table 5 Local recurrence after endoscopic resection for colorectal neoplasias ≥20 mm between EMR and ESD

Local recurrence rate			Procedures	Author
En bloc	Piecemeal	*P*-value		
3%	22%	<0.0001	EMR	Belderbos *et al*. (2014)[166]
2.3%	11.9%	<0.01	EMR	Oka *et al*. (2015)[53]
0.7%	13.9%	<0.01	ESD	Oka *et al*. (2015)[53]

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

Therefore, in the case of pT1 (SM) carcinoma after endoscopic treatment, not only local observation with colonoscopy but also periodic follow up should be systematically conducted using tumor markers such as carcinoembryonic antigen (CEA), cancer antigen (CA)19-9, abdominal ultrasonography, and thoracic, abdominal, and pelvic CT. However, no clear consensus has been reached on the actual method and time of surveillance.

Metachronous lesions

No optimal examination interval has been established to detect metachronous colorectal tumors. However, colonoscopy should be carried out within 3 years after endoscopic treatment (strength of recommendation: 2, level of evidence: C). Because metachronous lesions were reported in 30–60%

Table 6 Recurrence of pT1 carcinoma after endoscopic resection

No. of recurrences	Mean recurrence period	Author
n = 14	22.1 months (range: 2–66)	Yoshii *et al*. (2012)[167]
n = 8	53 months	Uragami *et al*. (2007)[168]
n = 24	29.7 months (IQR: 10.6–47.9)	Backes *et al*. (2017)[170]

IQR, interquartile range.

of cases,[173] metachronous lesions and residual lesions must be monitored. As colonoscopy might not be able to detect all lesions,[161,174,175] periodic endoscopic observation is essential. A multicenter retrospective cohort study[176] showed that a total of 193 (51%) lesions were newly diagnosed within 3 years; in particular, seven pT1(SM) cancers were detected in the first 12 months among 379 metachronous index lesions (adenoma >10 mm, intramucosal cancer, invasive cancer). This suggests that colonoscopy cannot detect all lesions, and high-quality examination should be done. The risk of metachronous advanced neoplasia[3] is known to be high in cases of multiple (>3) colorectal adenomas with lesions >10 mm in size and a history of colorectal carcinoma.[173,177] A pooled analysis of post-polypectomy patients showed that adjusted odds ratios of advanced neoplasia for those with villous features was 1.28 (95% CI: 1.07–1.52) and for those with high-grade dysplasia was 1.05 (95% CI: 0.81–1.35). Factors that were most strongly associated with the risk of advanced neoplasia were patient age and the number and size of prior adenomas.[178] Furthermore, certain risk factors for interval colorectal cancers[4] were reported.[179] A follow-up schedule must be established on the basis of each patient's background, including risk factors, age, and comorbidities. Multiple metachronous carcinomas have been reported in 0–26.5% of early colorectal carcinomas in the period between 25.6 and 102.8 months after endoscopic treatment for T1 carcinomas.[180–182] Therefore, long-term follow up should be considered. In the Western guidelines, follow up after endoscopic resection is stratified according to risk.[40,183] The JGES guidelines for colonoscopy screening and surveillance are being created.

PATHOLOGY

Handling of specimens

TO JUDGE CURABILITY of a lesion and the necessity for additional treatment, accurate histological diagnosis is critical, and resected specimens must be appropriately handled (level of evidence: VI, grade of recommendation: C1). The resected specimen is pinned on a rubber or cork sheet so that the mucous membrane surrounding the lesion is evenly flattened and the mucous membrane surface can be observed (Figs 2 and 3). Subsequently, the specimen is fixed with a 10–20% formaldehyde solution for 24–48 h at room temperature.[185] In addition, it is also recommended that fixation for 6–48 h is suitable for using molecular tests.[186]

As a specimen rapidly autolyzes after resection, it must be fixed as quickly as possible. To prevent drying of the specimen, it should be soaked in a normal saline solution. Thereafter, the endoscopist is required to appropriately display the specimen so that the difference between the specimen and clinical images is minimized, and the tumor margin of the specimen can be judged. Specimens obtained from piecemeal resection must be reconstructed to the greatest extent possible so that the tumor margin can be judged.

To conduct histological diagnosis precisely and in detail, specimens must be appropriately cut. An endoscopist must provide documentation (an explanatory text or an illustration) to a pathologist so that basic information on preoperative diagnosis (including the result of biopsy), site and morphology of the lesion, and tumor size as well as clinical evaluation can be accurately conveyed. It is helpful to indicate the location that most clearly shows the malignancy of the lesion in clinical and imaging findings in the aforementioned documentation.

After fixation, the specimen should be observed, sketched, and photographed using a ruler. The entire specimen is sectioned into pieces at intervals of 2–3 mm, and all slides are prepared for histological diagnosis. The procedure of actual cutting is as follows: (i) a tangent that touches the focus closest to the horizontal tumor margin is assumed, as shown in Figure 4; (ii) the first shallow cut is made in the direction perpendicular to the tangent; (iii) shallow cuts parallel to the first cut are made so that all slices are not completely separated from each other, after which the specimen is photographed; and (iv) deep cuts are made to completely separate all slices for preparation of slides. When a region of the lesion is unclear, observation with a stereoscopic microscope is recommended.[54]

Description of pathological findings

Histological diagnosis of tumors is carried out in accordance with the Japanese Classification of Colorectal Carcinoma (9th edition)[54] and the JSCCR guidelines 2019 for the treatment of colorectal cancer.[60] Histological type, depth of

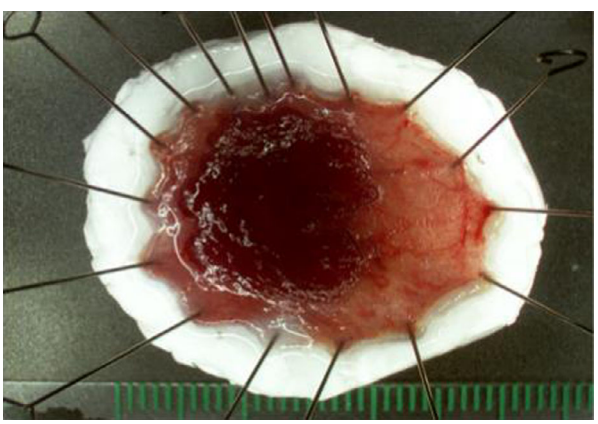

Figure 2 Fixed endoscopic mucosal resection specimen.

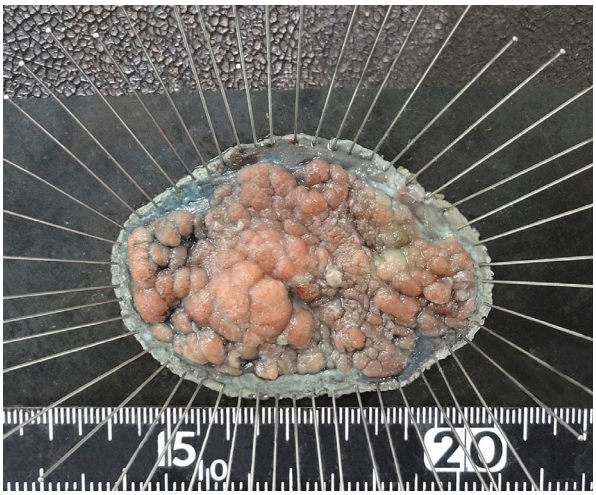

Figure 3 Fixed endoscopic submucosal dissection specimen.

invasion, vascular invasion (Ly, V), and resection of tumor margins (horizontal, vertical) of the carcinoma are judged. In the case of pT1 (SM) carcinoma, the invasion depth (pT1a: <1000 μm or pT1b: 1000 μm≤), tumor budding, amount of interstitial tissue, and pattern of invasion are also described.[54,185,187] When multiple different histological types are present in a tumor, all types are described in the decreasing order of area (e.g. tub1 > pap > por2). Depth of wall invasion is represented based on the deepest layer of carcinoma invasion. In the case of pT1 (SM) carcinoma, invasion depths of pedunculated and nonpedunculated lesions are separately evaluated.

Usefulness of special staining and immunostaining

For histological diagnosis, diagnosis of types with specialized histology, measurement of invasion depth, and special staining and immunostaining of vascular invasion are informative. With regard to types with specialized histology, endocrine cell carcinoma with a high grade of malignancy and carcinoid tumor with a low grade of malignancy/neuroendocrine tumor must be discriminated from adenocarcinoma. For this discrimination, immunostaining (chromogranin A, synaptophysin, and CD56) is effective. In the case of conventional adenocarcinoma, the grade of budding is assessed using hematoxylin-eosin (HE)-stained specimens. Cytokeratin is useful for histological evaluation because cancer cells become distinctive after immunostaining.[187,188] When measuring invasion depth, immunostaining with desmin helps identify the muscularis mucosae.[189,190] Elastica van Gieson staining or Victoria blue/HE double staining can be used to confirm venous invasion. To verify lymphatic vessel invasion, immunostaining with antilymphatic vessel endothelial antibody (D2-40) in combination with other staining methods is preferred.[187–193]

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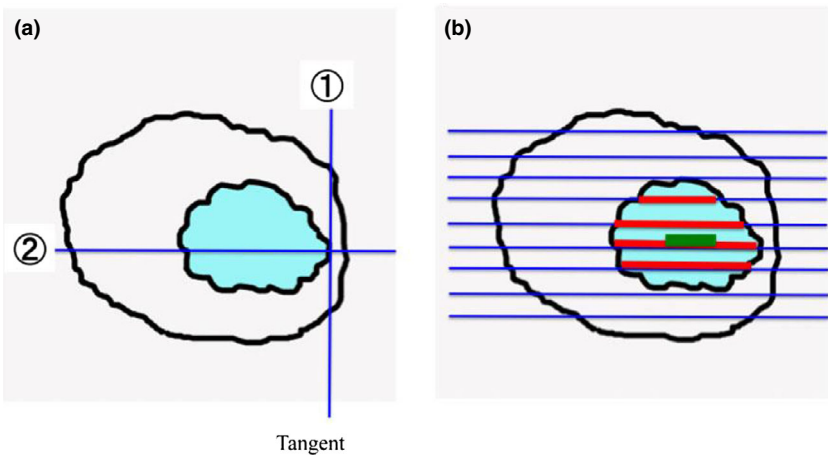

Figure 4 Cut-out of a resected specimen. (a) The direction of cut-out line; (b) the adequate parallel cut-out lines. —, mucosal cancer region; —, submucosal cancer region; ①, inadequate cut-out line; ②, adequate cut-out line.

oncologist (a total of 10) as members of the Guidelines Committee. Moreover, four gastroenterological endoscopists, and one gastroenterological pathologist (a total of five) were in charge of evaluating the Guidelines as members of the Evaluation Committee, as follows.

Guidelines Committee, Japan Gastroenterological Endoscopy Society

Responsible Director:
Kazuma Fujimoto (Department of Internal Medicine, Saga University Faculty of Medicine)
Chairman:
Kazuma Fujimoto (Department of Internal Medicine, Saga University Faculty of Medicine)
Working Committee
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Shinji Tanaka (Endoscopy and Medicine, Hiroshima University)
Chairman in charge of Guidelines creation:
Shinji Tanaka (Endoscopy and Medicine, Hiroshima University)
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Masahiko Watanabe (Department of Surgery, Kitazato University)
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Takashi Toyonaga (Division of Endoscopy, Kobe University Hospital)
Yoichi Ajioka (Division of Molecular and Diagnostic Pathology, Niigata University)

CONFLICTS OF INTEREST

AUTHOR H.K IS an Associate Editor of *Digestive Endoscopy*. Other authors declare no Conflict of Interests for this article.

Footnotes

[1] In Japan, the concept of intramucosal carcinoma (cancer; Tis) in the colorectum is accepted as it is globally established in the esophagus and the stomach. Intramucosal colorectal carcinoma in Japan is diagnosed based not only on structural atypia but also on cellular atypia, and it corresponds approximately to high-grade dysplasia in the Western world.

[2] Metachronous cancers: When two or more primary cancers are diagnosed over a period of a year or longer, they had been referred to as metachronous cancers. The period was revised to 2 months or longer in the 9th edition of Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma.[54]

[3] Advanced neoplasia: Advanced adenomas are defined as lesions >1 cm in size or with high-grade dysplasia or villous components. Advanced neoplasia is defined as an invasive cancer in addition to an advanced adenoma.

[4] Interval cancer: Interval cancer is defined as a "colorectal cancer diagnosed after a screening or surveillance examination in which no cancer is detected and before the date of the next recommended examination."[184] Post-colonoscopy colorectal cancer (PC-CRC) is used as a target of colonoscopy.

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