adenocarcinoma with high accuracy can be achieved (level of evidence: IVb, grade of recommendation: B). For distinction between adenoma and adenocarcinoma, 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 (indigocarmine, crystal violet etc.) and image-enhancement technology (narrow band imaging [NBI], blue laser imaging [BLI] etc.) could be used for diagnosing lesions on the basis of a detailed visualization of fine surface structures (surface pattern) and microvessels.[50–52] The diagnostic accuracy rate of discriminating neoplastic from non-neoplastic lesions was reported to be approximately 80% for standard observation, including magnifying chromoendoscopic observation, 96–98% for pit pattern observation, and 95% for magnifying observation using NBI and BLI.[53–59] The accuracy rate of discrimination between adenoma and carcinoma was 70–90% for pit pattern observation, and a similar rate was obtained for NBI. Thus, distinction between adenoma and adenocarcinoma with high accuracy can be achieved with magnifying endoscopic observation.[60–64] However, it was recently indicated that some lesions that had been previously diagnosed as non-neoplastic exhibited neoplastic proliferation (SSA/P). Research on the diagnosis and treatment of these lesions is currently ongoing.[65,66]

In addition, it is better to avoid carrying out a biopsy in order to distinguish between adenoma and adenocarcinoma (level of evidence: V, grade of recommendation: C1). In the case of superficial-type lesions, because biopsy as a preoperative diagnosis may cause fibrosis in the submucosal layer and lead to a positive non-lifting sign, subsequent endoscopic treatment will be difficult. Therefore, it is better to avoid carrying out a biopsy for making a preoperative diagnosis.[38,47] For large lesions such as LST-G,[44] which, in many cases, are 'carcinoma in adenoma', a simple biopsy may not show an accurate yield as a qualitative diagnosis. Therefore, a diagnosis based on 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 (level of evidence: IVb, grade of recommendation: B). The risks of vascular invasion and lymph node metastasis differ according to the SM invasion depth of the 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 carry out accurate pathological evaluation of endoscopically resected specimens, it is important to indicate the part of SM invasion in the whole lesion.[49]

When diagnosing invasion depth, if a deep depression, expansive appearance, submucosal 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%.[67,68] In pit pattern diagnosis with dye-spraying magnifying endoscopic observation, an accuracy rate of approximately 90% can be obtained if the V_N-type pit pattern is observed. The accuracy rate of protruded-type lesions tends to be slightly lower than that of superficial-type lesions.[69–71] Although magnifying observation using NBI/BLI is slightly inferior to pit pattern diagnosis in terms of accuracy, a similar outcome can be obtained.[72–74] The accuracy rate is approximately 80% when ultrasonography is used; however, the visualization capacity is affected by the condition and morphology of the lesion.[75–79] 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.

TECHNIQUES

Definition of ESD and EMR

IN EMR,[80,81] a physiological saline solution or a sodium hyaluronate solution[82–84] 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.

In ESD, a physiological 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 submucosal layer is then dissected. This technique can resect the lesion in one piece regardless of its size.[37,39,85–88] In April 2012 in Japan, the National Health Insurance scheme began offering coverage for expenses incurred for ESD procedures for early-stage malignant colorectal tumors 20–50 mm in size.

In the Guidelines, specific terminology is used to distinguish several forms of ESD, as follows. A technique in which dissection of the submucosal layer is completed without using a snare is defined as 'actual (narrowly defined) ESD'.[89,90] Likewise, a technique in which snaring is done without dissecting the submucosal 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'.[91] Finally, a technique in which the submucosal layer is dissected and snaring is carried out after the ESD procedure (mucosal incision + submucosal dissection), by using a knife for ESD or the tip of a snare, is defined as 'hybrid ESD'.[89,90,92] Other terminologies for precutting EMR[91] 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 carcinoma. However, piecemeal EMR is permissible for some adenoma and 'carcinoma in adenoma' lesions when appropriately carried out. When carrying out piecemeal EMR, magnifying endoscopic observation should be carefully carried out before the treatment, and the carcinomatous area should never be cut into pieces (level of evidence: III, grade of recommendation: B).

The reason for this restriction is that if SM invasive carcinoma was cut into pieces, pathological diagnosis for the invasion depth and lymph-vascular invasion would be difficult, and necessary additional treatment might not be done.[21,39,45,93,94] Previous reports showed that when piecemeal EMR was carried out, magnifying endoscopic observation of the lesion margin and ulcer base after the resection is useful to decrease the local residual/recurrence rate.[95] To confirm local residual/recurrence, follow-up colonoscopy should be done approximately 6 months after the treatment.[42,96–98]

The frequency of T1 (SM) carcinoma increases as the tumor size increases. With multi-piecemeal resection, which makes the pathological reconstruction of a tumor difficult, histological evaluation is also difficult and the local residual/recurrence rate is higher.[42,92,96,97] For large lesions with a size greater than half of the circumference of the colorectal lumen, piecemeal EMR should be avoided, and ESD or a surgical operation should be done based on the skill level of the endoscopist, the therapeutic environment of the hospital, the condition of patient, and the status of the lesion.[38,86,87]

Following the development of the requisite devices and the establishment of appropriate methods, colorectal ESD can be safely and accurately carried out by experts. However, when carrying out ESD, it is important to prepare various devices (ESD knives, devices, distal attachments, local injection agents such as sodium hyaluronate,[82–84] a carbon dioxide insufflator,[85] 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 non-lifting sign

Although the majority of such lesions are T1 carcinomas, a lesion exhibiting a positive non-lifting 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 (level of evidence: III, grade of recommendation: B).

For mucosal lesions that are non-lifting sign positive[99–101] (including adenomas) and residual/recurrence lesions, ESD can resect those lesions for which EMR is generally difficult to apply and for which en bloc resection is desirable (in particular, lesions suspected to be early carcinoma and LST-NG). However, ESD must be carefully carried out while checking for perforation.[37,45,102–104]

The non-lifting sign, first reported by Uno *et al.*,[99,100] is a sign that helps diagnose the depth of carcinoma invasion and is often used in clinical practice. However, one multicenter study[101] that compared the diagnostic accuracy based on conventional endoscopic observation with that based on the non-lifting sign has shown that the diagnostic ability of the non-lifting sign for deep SM invasive carcinoma had a sensitivity of 61.5%, specificity of 98.4%, positive predictive value of 80.0%, negative predictive value of 96.0%, and diagnostic accuracy of 94.8%.

For conventional endoscopic observation for deep SM invasive carcinoma, the above measures were 84.6%, 98.8%, 88.0%, 98.4%, and 97.4%, respectively. Therefore, conventional endoscopic observation was superior to the non-lifting sign in terms of sensitivity (84.6% *vs* 61.5%). Superficial-type colorectal tumors sometimes exhibit a positive non-lifting sign as a result of peristaltic motion or fibrosis caused by biopsy, although such lesions are usually of the mucosal type.[99,100] Therefore, preoperative endoscopic diagnosis should be made carefully by magnifying endoscopic observation before endoscopic treatment for neoplastic lesions. Once the lesion targeted is diagnosed as carcinoma, then 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 JGES or must possess skills similar to those of registered endoscopists in Japan. Familiarity with esophageal and gastric ESD alone may be insufficient. The minimum requirements for endoscopists are as follows: (i) having sufficient understanding of the anatomical features of the large intestine; (ii) having the ability to carry out the

axis-keeping shortening technique when inserting a colonoscope; (iii) having the skill to carry out an insertion technique by which the colorectal endoscope could be smoothly and accurately advanced to the cecum in the shortest distance possible; and (iv) having familiarity with the basic techniques of polypectomy, EMR, piecemeal 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.[105–107]

COMPLICATIONS DURING PROCEDURES

MAIN ACCIDENTAL COMPLICATIONS during colonoscopic treatment are perforation and bleeding. Perforation is the condition in which 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 in which 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. The presence of marked bloody stool after treatment or the requirement for a certain measure for hemostasis after treatment is often defined as delayed bleeding. With regard to the frequency of these accidental complications, perforation rates during endoscopic resection are reported to be 0.05%, 0.58–0.8%, and 2%–14% for polypectomy, EMR, and ESD, respectively. Moreover, the delayed bleeding rates are reported to be 1.6%, 1.15%–1.7%, and 0.7%–2.2% for polypectomy, EMR, and ESD, respectively.[40,88,108–110]

Prevention and management of perforation

As the colonic wall is thinner than that of the stomach, the risk of perforation during the procedure is higher in the colon than in the stomach. Before the procedure, sufficient pretreatment 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.[85,111] When perforation occurs during the procedure, clipping should be carried out as far as possible, regardless of the location (level of evidence: IVb, grade of recommendation: B). When closure of the perforation is complete, surgical rescue can usually be avoided by giving i.v. antibiotics and fasting.[108,112,113] 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.[113] It is necessary to decide the timing of the emergency surgery carefully 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 this situation.

In cases of rectal lesion below the peritoneal reflection, perforation into the abdominal cavity would not occur as a result of anatomical features; however, penetration into the retroperitoneum occurs and, consequently, mediastinal emphysema or subcutaneous emphysema may occur.[114]

Prevention and management of bleeding

For bleeding associated with endoscopic resection, clipping or coagulation is appropriate. In case of minor bleeding from a small vessel, contact coagulation with the tip of a knife 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. Generally, severe bleeding seldom occurs in the colon in comparison with the stomach. However, in the rectum, especially below the peritoneal reflection, a pulsating large exposed vessel is sometimes present within the resection wound. Therefore, clipping is sometimes used in such cases to prevent delayed bleeding. Serious delayed bleeding that requires blood transfusion seldom occurs in the colon. Emergency endoscopy is usually required to treat exposed blood vessels in the case of continuous bloody stool.

A randomized controlled trial reported that preventive clipping after endoscopic resection did not decrease the delayed bleeding rate (0.98% with clipping and 0.96% without clipping).[115] However, target lesions included in that trial were relatively small (mean size, 7.8 mm). A retrospective analysis reported that preventive clipping was useful for lesions >2 cm in size (1.8% with clipping and 9.7% without clipping).[116] Another retrospective analysis also suggested the potential usefulness of preventive clipping for patients undergoing endoscopic resection at an outpatient clinic.[117] However, at present, no firm evidence has been obtained by randomized controlled trials for the efficacy of suturing the ESD/EMR wound to prevent delayed bleeding. In addition, one report showed that preventive clipping after polypectomy is poorly cost-effective in subjects who are not taking antithrombotic medication.[118] Therefore, prophylactic clipping in EMR seems to be effective to some extent for high-

risk patients and may be effective for patients with large lesions or for those undergoing antithrombotic therapy (level of evidence: IVb, grade of recommendation: B).

PERIOPERATIVE CARE BEFORE AND AFTER ENDOSCOPIC TREATMENT

DURING PERIOPERATIVE CARE after endoscopic treatment, attention should be given to delayed perforation and delayed bleeding, and patients should be hospitalized if necessary (level of evidence: IVb, grade of recommendation: B). Perioperative care should be considered during the clinical practice of ESD/EMR, including the hospitalization period.[119] 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 the JGES.[2]

Antithrombotic drugs

The guidelines mentioned above propose a strategy in which 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 for thromboembolism in subjects, and published JGES guidelines should be referred to for further details. In brief, withdrawal of aspirin monotherapy even in subjects who undergo ESD/EMR is not required when those subjects are deemed at high risk for thromboembolism, whereas it can be withdrawn for 3–5 days in low-risk patients. Thienopyridine derivatives are recommended to be replaced with aspirin or cilostazol for 5–7 days in high-risk subjects who undergo ESD/EMR procedures. However, in low-risk subjects, thienopyridine derivatives can be withdrawn for 5–7 days for the procedures. The procedures planned in patients taking aspirin in combination with warfarin or dabigatran should be postponed until the antithrombotics can be withdrawn. The procedures can be carried out in patients taking aspirin or cilostazol if warfarin or dabigatran is replaced with heparin. After the withdrawal of an antithrombotic drug, the drug can be given again when hemostasis is endoscopically confirmed. Careful observation against post-procedure hemorrhage must be taken after antithrombotic drugs are resumed.

Bowel preparation

After confirming that no stenosis of the digestive tract is present, 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 L of an intestinal lavage solution is given. In cases where pretreatment is incomplete, an additional intestinal lavage should 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. The use of a sedative/analgesic is determined according to the endoscopist's judgment and the patient's wishes. 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, decreasing the amount of sedatives required.[85,111]

Instruments and drugs to be prepared

When a sedative is used during the procedure or when treatment is predicted to take a considerable time, it is desirable to monitor the patient's oxygen saturation and electrocardiogram.

Postoperative management

In the Japanese situation, EMR for lesions <2 cm in size can be carried out for outpatients. 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. One report regarding ESD found that no adverse event occurred in a clinical pathway where the length of hospitalization was 4 nights and 5 days with oral ingestion starting 2 days after the operation.[119] A meal is given after confirming the absence of inflammatory findings, such as level of serum C-reactive protein (CRP), 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 sometimes occurs after electrocoagulation, even when no subsequent perforation occurs.[120] 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 an intestinal perforation that develops a certain period of time after the operation (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 the operation. However, approximately one-third of delayed perforation cases are confirmed 24 h after the treatment. Free air, which cannot be detected by simple X-ray imaging, is sometimes found 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 (i.e. indicating that delayed perforation seldom occurs).[37,88,121]

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.[122] Delayed bleeding does not include small amounts of bleeding such as the presence of trace amounts of blood in the stool. The incidence of delayed bleeding is reported to be 1.4–1.7% in EMR[88,97] and 1.5–2.8% in ESD.[37,88,97,121] Delayed bleeding is mainly observed during the period between 2 and 7 days after the operation, and a hemorrhage observed within 10 days after the operation may be considered delayed bleeding. The 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.[123] However, the effectiveness of prophylactic clip application for high-risk lesions must be evaluated through prospective studies.

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.[114] 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.[124] 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.[125]

ASSESSMENT OF CURABILITY

CURABILITY IS EVALUATED based on the tumor margin of the resected specimen and risk factors for lymph node/distant metastasis (level of evidence: IVb, grade of recommendation: B).

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 local resection. However, in cases with positive lateral tumor margin or piecemeal resection, local recurrence has been reported.[42,124,126] Previous reports have compared the rates of en bloc resection in EMR (piecemeal EMR) with those in ESD for mucosal lesions with tumor sizes <20 mm and >20 mm. Consequently, the rates of en bloc resection were determined to be as high as 66.5–80% in EMR when the tumor sizes were <20 mm.[88,127] When the tumor sizes were ≥20 mm, the en bloc resection rate in EMR decreased as tumor size increased, and the residual/recurrence rate was 2.7–27.2%.[125,128] In contrast, the en bloc resection rate in ESD was within the range of 84–94.5% (i.e. the results were excellent).[35,39,88,92,125,128]

T1 (SM) carcinoma

When pT1 (SM) carcinoma is detected in a pathological examination after endoscopic treatment, the subsequent therapeutic course should be determined in accordance with the 2014 JSCCR Guidelines for the Treatment of Colorectal Cancer.[129] An additional surgical operation should be carried out for deep tumor margin-positive lesions as a result of incomplete endoscopic resection. In the case of complete endoscopic resection, pT1 (SM) carcinoma 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). If even one of these five conditions is not satisfied, 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 an operation that includes factors such as the construction of an artificial anus) are comprehensively evaluated and the indication for additional surgical resection is considered. 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.

When a resected specimen satisfies the five conditions mentioned above, lymph node metastasis and residual/

recurrence is extremely rare (level of evidence: IVb, grade of recommendation: B). In cases in which only the SM invasion depth does not satisfy the criteria for a radical cure, and where no other risk factors for metastasis are observed, the lymph node metastasis rate has been reported to be extremely low.[130–134] At present, a research project of JSCCR concerning the stratification of risk factors for the metastasis of pT1b SM cancer (SM invasion depth >1000 μm) to other organs is ongoing.

POSTOPERATIVE FOLLOW UP

THE AIM OF follow up after colorectal ESD/EMR is early detection of local residual/recurrence, metastasis, and metachronous lesions.[133,134] Some studies have reported that endoscopic treatment for colorectal tumors decreased the incidence of colorectal carcinoma and the risk of mortality.[135,136] Surveillance after surgical resection for colorectal carcinoma was reported to improve prognosis.[137,138] Although no evidence-based consensus on the actual follow-up methods after endoscopic treatment is available in Japan, the JSGE 'Evidence-Based Clinical Guidelines for Management of Colorectal Polyps (in press)' guidelines recommend that follow-up colonoscopy should be done within 3 years after polypectomy.[139] 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 the 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 many early detection cases. In adenoma or pTis (M) carcinoma, when piecemeal resection is used or the tumor margin after resection is unclear and the curability cannot be accurately evaluated, colonoscopy should be done approximately 6 months after the endoscopic treatment (level of evidence: IVb, grade of recommendation: B). Compared with complete en bloc resection, histological evaluation is more difficult and the local residual/recurrence rate is higher in piecemeal resection.[42,92,96,140,141] The recurrence rates were reported to be 18.4%, 23.1%, and 30.7% at 5, 12, and 24 months after piecemeal resection, respectively.[96] When the horizontal tumor margin is difficult to evaluate or when piecemeal resection is carried out, it is recommended to carry out colonoscopy within 6–12 months.[49,142]

No local residual/recurrence was detected in the case of adenoma or pTis (M) carcinoma for which complete en bloc resection had been carried out and for which curative resection was concluded based on histological examination.[49,129] However, in the case of pT1a (SM) carcinoma (SM invasion depth <1000 μm), histological evaluation of vascular invasion and SM invasion depth cannot be accurately carried out as resected specimens are inadequately handled; consequently, local residual/recurrence may occur. Although such cases are rare, careful handling of resected specimens must be ensured.

Recurrence or metastasis of pT1 (SM) carcinoma occurs even in cases where surgical resection including lymph node dissection has been carried out. The recurrence rate in the rectum (4.2–4.5%) is higher than in the colon (1.5%–1.9%).[143,144] In the case of endoscopic treatment, recurrence or metastasis is reported to occur mainly within 3–5 years.[130,132,134,145] 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 carried out using tumor markers such as carcinoembryonic antigen (CEA), abdominal ultrasonography, and thoracic and abdominal 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 (level of evidence: IVb, grade of recommendation: B). After endoscopic treatment, metachronous lesions and residual lesions must be monitored. As colonoscopy might not be able to detect all lesions,[133,146,147] periodic endoscopic observation is essential. A retrospective surveillance study[148] showed that after endoscopic treatment for T1 carcinoma, metachronous adenoma and early carcinoma were detected in 54.8% and in 11.9% of cases, respectively. This suggests that colonoscopy cannot detect all lesions. Multiple metachronous carcinomas were reported in 3.4–26.5% of early colorectal carcinomas in the period between 25.6 and 102.8 months after endoscopic treatment for T1 carcinomas.[148,149] Therefore, long-term follow up should be considered. The risk of metachronous colorectal tumors is known to be high in cases of multiple (>3) colorectal adenomas with lesions >10 mm in size and a history of colorectal carcinoma.[146,150–152] A follow-up schedule must be established on the basis of each patient's background, including risk factors, age, and comorbidities. In the USA, follow up after endoscopic resection is stratified according to risk, and colonoscopy is recommended to be carried out for multiple (3–10) adenomas, adenomas >10 mm in size, villous adenomas, and high-grade dysplasia 3 years after endoscopic treatment. Moreover, colonoscopy is recommended to be carried out for multiple (>10) adenomas within 3 years after endoscopic treatment.[142]

PATHOLOGY

Handling of specimens

TO JUDGE THE 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 recommendations: 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 2,3). Subsequently, the specimen is fixed with a 10–20% formaldehyde solution for 24–48 h at room temperature.[153]

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 physiological saline solution. Thereafter, the endoscopist is required to appropriately display the specimen so that the difference between the specimen and the 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.

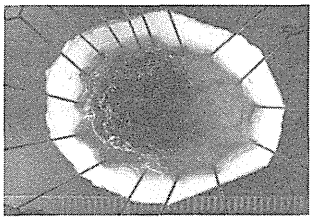

Figure 2 Fixed endoscopic mucosal resection specimen.

To carry out histological diagnosis precisely and in detail, specimens must be appropriately cut (level of evidence: VI, grade of recommendation: C1). An endoscopist must provide documentation (an explanatory text or an illustration) to a pathologist so that the basic information on preoperative diagnosis (including the result of biopsy), the site and morphology of the lesion, and the tumor size as well as the clinical evaluation can be accurately conveyed. It is helpful to indicate the location that most clearly exhibits the malignancy of the lesion in clinical and imaging findings in the above documentation.

After fixation, the entire specimen is sectioned into pieces at intervals of 2–3 mm, and all slides are prepared for histological diagnosis. Procedure of the actual cutting is as follows: (i) a tangent that touches the focus closest to the horizontal tumor margin is assumed, as shown in

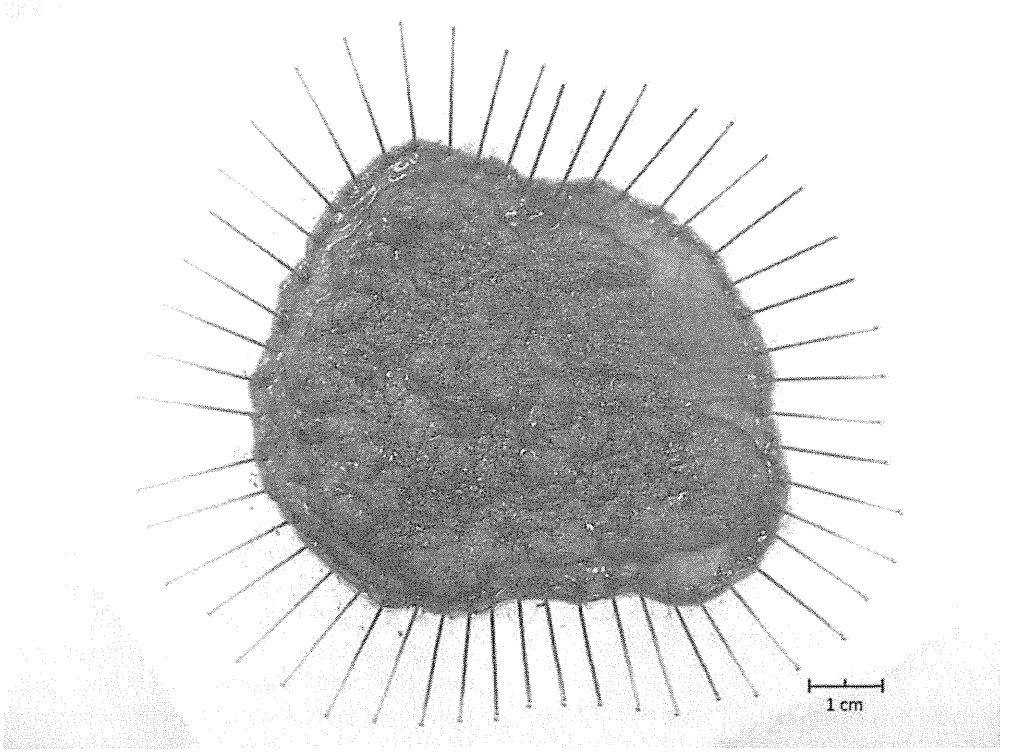

Figure 3 Fixed endoscopic submucosal dissection specimen.

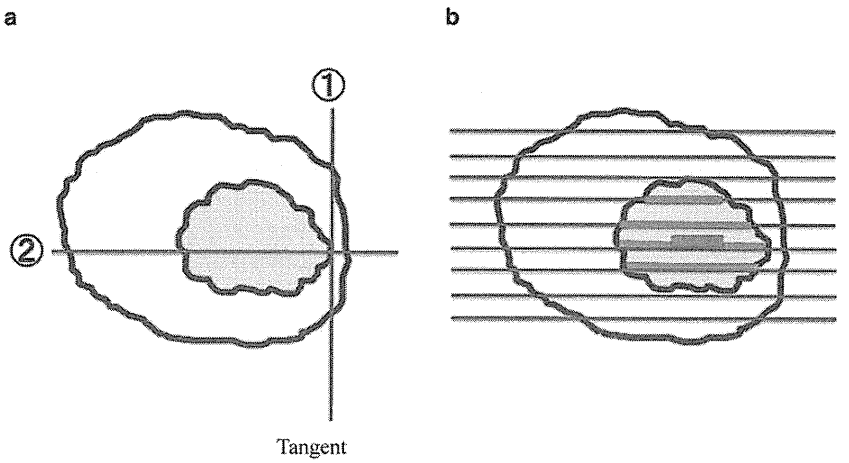

Figure 4 Cut-out of a resected specimen. —, mucosal cancer region; —, submucosal cancer region.

Figure 4; (ii) the first shallow cut is carried out in the directionperpendicular to the tangent; (iii) shallow cuts parallel to the first cut are carried out so that all slices are not completely separated from each other, after which the specimen is photographed; and (iv) deep cuts are carried out to completely separate all the slices for the preparation of slides. When a region of the lesion is unclear, observation with a stereoscopic microscope is recommended.[44]

Description of pathological findings

Histological diagnosis of tumors is carried out in accordance with the *Japanese Classification of Colorectal Carcinoma* (8th edition).[44] The histological type, depth of wall invasion, vascular invasion (ly, v), and resection 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.[44,153,154] When multiple different histological types are present in a tumor, all the types are described in decreasing order of area (e.g. tub1>pap>por2). The depth of wall invasion is represented based on the deepest layer of carcinoma invasion. In the case of pT1 (SM) carcinoma, the invasion depths of pedunculated and non-pedunculated lesions are evaluated separately.

Usefulness of special staining and immunostaining

In 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.[154,155] When measuring the invasion depth, immunostaining with desmin helps to identify the muscularis mucosae.[156,157] Elastica van Gieson staining or Victoria blue/HE double staining can be used to confirm venous invasion. To verify lymphatic vessel invasion, immunostaining with anti-lymphatic vessel endothelial antibody (D2-40) in combination with other staining methods is preferred.[154–160]

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Guidelines Committee, Japan Gastroenterological Endoscopy Society

Responsible Director:
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Chairman:
Kazuma Fujimoto (Department of Internal Medicine, Saga University Faculty of Medicine)
Working Committee
Chairman:
Shinji Tanaka (Endoscopy and Medicine, Hiroshima University)
Chairman in charge of Guidelines creation:
Shinji Tanaka (Endoscopy and Medicine, Hiroshima University)
Deputy Chairman:
Hiroshi Kashida (Department of Gastroenterology and Hepatology, Kinki University Faculty of Medicine)
Members:
Yutaka Saito (Endoscopy Division, National Cancer Center Hospital)
Naohisa Yahagi (Tumor Center, Keio University Hospital)
Hiroo Yamano (Digestive Disease Center, Akita Red Cross Hospital)
Shoichi Saito (Department of Endoscopy, The Jikei University School of Medicine)
Takashi Hisabe (Department of Gastroenterology, Fukuoka University Chikushi Hospital)
Takashi Yao (Department of Pathology, Juntendo University)
Masahiko Watanabe (Department of Surgery, Kitazato University)
External member: Masahiro Yoshida (Chemotherapy Institute, Kaken Hospital)
Chairman of the Evaluation Committee:
Shin-ei Kudo (Digestive Disease Center, Showa University Northern Yokohama Hospital)
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Osamu Tsuruta (Digestive Disease Center, Kurume University School of Medicine)
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Yoichi Ajioka (Division of Molecular and Diagnostic Pathology, Niigata University)

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Impact of revisions of the JSCCR guidelines on the treatment of T1 colorectal carcinomas in Japan

Auswirkungen von Änderungen der JSCCR-Leitlinien für die Behandlung von kolorektalen T1-Karzinomen in Japan

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Schlüsselwörter
- kolorektale T1-Karzinome
- Fragebogen
- endoskopische Resektion
- zusätzliche chirurgische Resektion
- JSCCR-Richtlinien 2005
- JSCCR-Richtlinien 2009/10

Key words
- T1 colorectal carcinoma
- questionnaires
- endoscopic resection
- additional surgical resection
- JSCCR guideline 2005
- JSCCR guideline 2009/10

Zusammenfassung

Ziel: Im Jahr 1977 veröffentlichte die Japanese Society for Cancer of the Colon and Rectum (JSCCR) die erste Ausgabe der allgemeinen Leitlinien über die Dokumentation von histopathologischen Befunden und die Behandlung kolorektaler Karzinome (KRK). Seitdem wurden die Leitlininen mehrfach überarbeitet. Ziel dieser Studie war es, den Einfluss der Revisionen der JSCCR-Leitlinien auf die Behandlung von KRKs der Submukosa (T1-Karzinome) im klinischen Umfeld in Japan zu untersuchen.

Methoden: An alle 391 Mitgliedseinrichtungen der JSCCR wurden Fragebögen versandt. Diese bestanden aus zwei Teilen: genaue Angaben zur Einrichtung und Behandlungsstrategien für T1-Karzinome.

Ergebnisse: 73 Institutionen (19 %) beantworteten die Umfrage. Die Anzahl der behandelten T1-Karzinome hat jedes Jahr zugenommen und der Anteil der endoskopischen Resektionen von T1-Karzinomen ist mit den Revisionen der Leitlinien signifikant gestiegen (1417 [47 %] von 2985 T1-Karzinomen in den Jahren 2003 – 2005, 2110 [50 %] von 4212 in den Jahren 2006 – 2008, und 2546 [54 %] von 4686 in den Jahren 2009 – 2011, P<.05).

Schlussfolgerung: Die Revisionen der JSCCR-Leitlinien haben die Behandlung von kolorektalen T1-Karzinomen im klinischen Umfeld in Japan beeinflusst. Die Überprüfung der Kriterien für kurative endoskopische Resektionen wäre wünschenswert, um überflüssige Eingriffe zu vermeiden.

Abstract

Purpose: In 1977, the Japanese Society for Cancer of the Colon and Rectum (JSCCR) published the first edition of the general guidelines that described how to record clinical and histopathological findings of colorectal carcinomas (CRCs) and how to treat these cancers, and since then, the guidelines were revised several times. The aim of this study was to examine the impact of the revisions of the JSCCR guidelines on the treatment of submucosal CRCs (T1-CRCs) in Japanese clinical settings.

Methods: Questionnaires were sent to all 391 member institutions of the JSCCR. The questionnaires consisted of 2 parts: details of the institutions and treatment strategies for T1-CRCs.

Results: 73 (19 %) institutions responded to the survey. The number of treated T1-CRCs has increased year by year, and the rate of endoscopic resection for T1-CRCs has significantly increased with revisions of the guidelines (1417 [47 %] of 2985 T1-CRCs in 2003 – 2005, 2110 [50 %] of 4212 in 2006 – 2008, and 2546 [54 %] of 4686 in 2009 – 2011, *P*<.05).

Conclusion: The revisions of the JSCCR guidelines have influenced the treatment of T1-CRCs in Japanese clinical settings. There is room to revise the criteria for curative endoscopic resection to avoid unnecessary surgeries.

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Introduction

Colorectal carcinoma (CRC) is a major cause of death in Japan, as in Western countries, accounting for the greatest number of deaths from malignant neoplasms in women and the third greatest number in men [1]. The widespread use of colonoscopy enables the detection of many early-stage CRCs [2, 3], and the progress in endoscopic diagnostic [4 – 6] and treatment [5 – 8] methods has allowed resection of mucosal (Tis) and submucosal (T1) CRCs in a complete en bloc manner. However, there are disparities in the medical care provided nationwide in Japan to patients with

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SPECIAL ARTICLE

Comprehensive Registry of Esophageal Cancer in Japan, 2007

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Published online: 1 March 2015

Preface 2007

We deeply appreciate the great contributions of many physicians in the registry of esophageal cancer cases. The Comprehensive Registry of Esophageal Cancer in Japan, 2007, was published here, despite some delay. The registry complies with the Act for the Protection of Personal Information. The encryption with a HASH function is used for ''anonymity in an unlinkable fashion''.

These data were first made available on December 25, 2014, as the Comprehensive Registry of Esophageal Cancer in Japan, 2008. Not all the pages are reprinted here; however, the original table and figure numbers have been maintained.

The authors were members of the Registration Committee for Esophageal Cancer, the Japan Esophageal Society, and made great contributions to the preparation of this material.

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We briefly summarized the Comprehensive Registry of Esophageal Cancer in Japan, 2007. Japanese Classification of Esophageal Cancer 10th and UICC TNM Classification 6th were used for cancer staging according to the subjected year. A total of 5216 cases were registered from 257 institutions in Japan. Tumor locations were cervical: 4.4 %, upper thoracic: 12.7 %, middle thoracic: 49.5 %, lower thoracic: 25.1 % and EG junction: 5.9 %. Superficial carcinomas (Tis, T1a, and T1b) were 35.7 %. As for the histologic type of biopsy specimens, squamous cell carcinoma and adenocarcinoma accounted for 90.1 % and 3.9 %, respectively. Regarding clinical results, the 5-year survival rates of patients treated using endoscopic mucosal resection, concurrent chemoradiotherapy, radiotherapy alone, chemotherapy alone, or esophagectomy were 88.1, 25.1, 16.0, 9.4, and 52.8 %, respectively. Esophagectomy was performed in 2834 cases. Concerning the approach used for esophagectomy, 19.8 % of the cases were treated thoraco-

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SPECIAL ARTICLE

Comprehensive Registry of Esophageal Cancer in Japan, 2008

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Preface 2008

We deeply appreciate the great contributions of many physicians in the registry of esophageal cancer cases. The Comprehensive Registry of Esophageal Cancer in Japan, 2008, was published here, despite some delay. The registry complies with the Act for the Protection of Personal Information. The encryption with a HASH function is used for ''anonymity in an unlinkable fashion''.

We briefly summarized the Comprehensive Registry of Esophageal Cancer in Japan, 2008. Japanese Classification of Esophageal Cancer 10th and UICC TNM Classification 6th were used for cancer staging according to the subjected year. A total of 4925 cases were registered from 257 institutions in Japan. Tumor locations were cervical: 5.3 %, upper thoracic: 12.0 %, middle thoracic: 48.7 %, lower thoracic: 25.3 % and EG junction: 5.9 %. Superficial carcinomas (Tis, T1a, and T1b) were 35.3 %. As for the histologic type of biopsy specimens, squamous cell carcinoma and adenocarcinoma accounted for 89.3 % and 4.3 %, respectively. Regarding clinical results, the 5-year survival rates of patients treated using endoscopic mucosal resection, concurrent chemoradiotherapy, radiotherapy alone, chemotherapy alone, or esophagectomy were 85.7, 24.1, 23.4, 4.8, and 53.1 %, respectively. Esophagectomy was performed in 2657 cases. Concerning the approach used for

These data were first made available on December 25, 2014, as the Comprehensive Registry of Esophageal Cancer in Japan, 2008. Not all the pages are reprinted here; however, the original table and figure numbers have been maintained.

The authors were members of the Registration Committee for Esophageal Cancer, the Japan Esophageal Society, and made great contributions to the preparation of this material.

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ORIGINAL ARTICLE

A nation-wide survey of follow-up strategies for esophageal cancer patients after a curative esophagectomy or a complete response by definitive chemoradiotherapy in Japan

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Abstract

Background There is a lack of critical evidence to justify the methods of follow-up after a curative esophagectomy or a complete response to definitive chemoradiotherapy (dCRT). Consequently, a wide variety of practices are in place throughout the world.

Methods A questionnaire concerning follow-up protocols was sent via electronic email for a nation-wide survey of the 117 Japanese hospitals that are recognized by the Japan Esophageal Society as training facilities for certified esophageal surgeons. Seventy-seven hospitals responded to the questionnaire.

Results Most hospitals follow their patients for at least 5 years after esophagectomy or dCRT, usually at a frequency of more than 4 times per year with clinical visits and physical examinations in the 1st and 2nd year after treatment. About 65–75 and 40 % of the hospitals continue the follow-up until the 7th and 10th year after treatment, respectively. Most hospitals measure CEA and SCC-Ag and almost all hospitals utilize CT scans of the cervix, chest and abdomen for the follow-up. Most of the hospitals reported performing an upper gastrointestinal endoscopy at least once per year until the 5th year after treatment, more frequently for post-dCRT patients than for post-esophagectomy patients. Other imaging modalities such as FDG-PET/

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CT, cervical and abdominal USs, and chest and abdominal X-rays were incorporated at much lower rates.
Conclusions Follow-up protocols for patients who have been treated for esophageal cancer with curative intent vary among the hospitals in Japan. Based on these data, the most popular follow-up protocols in Japan are shown.

Keywords Esophageal cancer · Curative esophagectomy · Definitive chemoradiation · Recurrence · Follow-up strategies · Nation-wide survey

Abbreviations

dCRT	Definitive chemoradiotherapy
CR	Complete response
QOL	Quality of life
CV	Clinical visit
CT	Computed tomography
CEA	Carcinoembryonic antigen
SCC-Ag	Squamous cell carcinoma antigen
p53-Ab	p53 antibody
FDG-PET	Positron emission tomography with ^{18}F-fluorodeoxyglucose
UGIE	Upper gastrointestinal endoscopy
US	Ultrasonography
Xp	Plain X-ray

Introduction

Despite the recent improvements in the treatment outcome of esophageal cancer patients who are treated with multimodality therapies including esophagectomy with lymph node dissection or definitive chemoradiotherapy (dCRT), post-treatment recurrence occurs in a considerable number of patients [1–4]. Curative treatments of recurrence are necessary to further improve the prognosis of patients after such treatments with curative intent, although achieving a successful cure in patients with recurrence remains rare, even after multimodality therapies. However, critical evidence to justify the treatment strategies for cases of recurrence and the methods of follow-up to diagnose recurrence after the initial treatment with curative intent is still lacking in Japan [5] and Western countries [6–8]; consequently, a wide variety of practices are in place throughout the world.

The primary aim of follow-up after a curative resection of esophageal cancer or obtaining a complete response (CR) by dCRT is to detect local recurrence, distant metastases or metachronous primary cancers at an early stage when curative treatments are still possible, thus leading to an improvement of the prognosis. Follow-up is also important for evaluating and managing the patient's general status and quality of life (QOL), because esophagectomy and dCRT are associated with a significant level of postoperative complications and late toxicities, such as pleural or pericardial effusion [9]. The following questions should be considered when determining follow-up protocols after treatments with curative intent for esophageal cancer: (1) what is the best combination of modalities for diagnosing recurrences at an early stage? (2) Does the early detection of recurrence lead to the elongation of survival or QOL improvement? (3) What methods are the most effective from an economical point of view?

Several recommendations for follow-up after a curative resection or dCRT for esophageal cancer are noted in the guidelines of the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO), although no references that show evidence are cited [10, 11]. Large-scale clinical trials that address follow-up methods after esophageal cancer treatment seem difficult to design, because the choice of the initial treatment varies markedly, depending on the stage of the disease and the patient's general condition at the time of diagnosis. Instead, large-scale data collection based on some form of consensus protocol(s) might answer the above-mentioned questions. At present, however, consensus follow-up protocols are still a long way from being established. Moreover, it appears to be hard to directly adapt the data from the Western countries to the Japanese patients with esophageal cancer, because there are considerable differences in the predominant histology and tumor locations, the surgical methods used and the survival rates after surgery between patients in Japan and those in the Western countries [12].

The aims of the present study are to investigate the current follow-up practices after treatments with curative intent for patients with esophageal cancer using a nation-wide survey in Japan and to attempt to create a consensus follow-up protocol.

Materials and methods

In October 2014, a questionnaire was sent via electric mail, as a nation-wide survey of 117 hospitals that are recognized by the Japan Esophageal Society (JES) as training facilities for certifying specialized esophageal surgeons. By December 15, 2014, answers were obtained from 77 hospitals (65.8 %) (Online Resource 1).

The questionnaire included the numbers of hospital beds, newly registered esophageal cancer patients per year and certified esophageal surgeons. Online Resource 2 shows the backgrounds of the hospitals that responded to the questionnaire. Sixty-seven (88.2 %) of the hospitals have more than 500 beds (Online Resource 2A). Online Resources 2B and 2C show the numbers of esophageal cancer patients per year and JES-certified esophageal surgeons in each hospital, respectively. At the time of the survey there were 207 JES-certified esophageal surgeons in Japan.

In Japan, dCRT was conducted by surgeons, radiation oncologists and either of them in 43, 39 and 18 %, respectively. The follow-up after dCRT was done in a similar proportion. Anti-cancer chemotherapy was performed by surgeons or medical oncologists in 52 or 25 % of the hospitals, respectively. Terminal care is also given by surgeons in 44 % of the hospitals in Japan (Online Resource 3).

The modalities used for follow-up after a curative esophagectomy or CR by dCRT in each hospital were investigated, these included: clinical visits (CVs) for anamnesis and physical examination, tumor markers (carcinoembryonic antigen: CEA, squamous cell cancer antigen: SCC-Ag, others), chest plain X-ray (Xp), abdominal Xp, cervical-chest and abdominal-pelvic computed tomography (CT), cervical ultrasound (US), abdominal US, positron emission tomography with ^{18}F-fluorodeoxyglucose (FDG-PET), bone scintigraphy, upper gastrointestinal endoscopy (UGIE), colonoscopy or colonography, screening of head and neck (H&N) region and the assessment of QOL. The frequency and duration of each modality were investigated for 10 years after the initial treatment.

The protocols for the patients with Stage 0/I and Stage II/III/IV (pathological stages for esophagectomy and clinical stages for dCRT) [13, 14] were separately assessed for each of curative esophagectomy and dCRT, because there are apparent differences in the survival rates between Stage I and Stage II in Japan [15].

Results

Seventy-seven hospitals responded to the questions on post-esophagectomy protocols and 73 responded to the questions on post-dCRT protocols. Thirty-five (44.5 %) of 77, and 35 (47.9 %) of 73 hospitals reported that they utilized the same follow-up protocols after esophagectomy or dCRT, respectively, regardless of stage.

Clinical visits for anamnesis and physical examination

The frequencies of CVs for anamnesis and physical examination in the subsequent years after esophagectomy and dCRT are shown in Fig. 1. Most of the hospitals reported that they followed their patients more than 4 times in the 1st year after either treatment. Seventy-four percent and 68 % of the hospitals reported that they performed CVs for patients with Stage II/III/IV at least 4 times a year, even in the 3rd year, after esophagectomy and dCRT, respectively. All hospitals continued CVs for all stages until the 5th year after treatment. Even in the 5th year, most hospitals followed the patients of any stage at least twice a year. Roughly speaking, one-fourth of the hospitals reported that they terminated their follow-ups after 5 years, while about 40 % reported that they performed a CV once or twice a year until the 10th year, after either treatment. For the patients of Stage 0/I, CVs were performed slightly less frequently (for both treatments) in the first 5 years than those for Stage II/III/IV (Fig. 1).

Measurements of tumor markers

Nearly all of the hospitals reported that they measured CEA and SCC-Ag for at least 5 years after treatments with curative intent (Online Resource 4). These markers were mostly measured at the same time. With the exception of the 1st year, the frequency and duration of the measurements were similar (Online Resources 5 and 6).

Other than CEA and SCC-Ag, cyfra (cytokeratin 19 fragment), p53 antibody (p53-Ab) and CA19-9 were incorporated in the follow-up protocols of some of the hospitals (Online Resource 4). When incorporated, the frequencies of measurement were similar to the frequencies of measurement of CEA and SCC-Ag (data not shown).

Routine imaging modalities

Ninety-four percent of the hospitals reported that they utilized CT scans ranging from the cervix to the pelvis (or sometimes of the upper abdomen instead) in their follow-up protocols after treatments with curative intent (Fig. 2; Online Resource 7). In the 1st year after esophagectomy and dCRT, about 90 % of the hospitals reported performing CT at least twice, while 54 and 74 % reported performing CT 3 or 4 times a year for Stage II/III/IV after esophagectomy and dCRT, respectively. Eighty-seven percent and 92 % of the hospitals performed CT for Stage II/III/IV more than twice a year even in the 3rd year after esophagectomy and dCRT, respectively. Most hospitals continued performing CT scans until the 5th year. Roughly speaking, about 60 and 30 % of the hospitals continued performing CT scans for Stage II/III/IV patients until the 7th and 10th years after treatment, respectively. The post-dCRT follow-up seemed to be more intensive than the post-esophagectomy follow-up during the 5-year period. A small number of the hospitals, most of which incorporated FDG-PET in their protocols, did not utilize CTs (data not shown). Including these hospitals, 20–30 % reported that they utilized FDG-PET/CT examinations for follow-up at least 5 years after treatment (Online Resource 8).

Chest Xp was only utilized in only the 1st year after esophagectomy and dCRT for Stage II/III/IV patients in 32 and 21 % of the hospitals, respectively; and in only 5–10 % in the 2nd year and thereafter. Abdominal Xp was performed less frequently. Cervical and abdominal USs were incorporated in 11–13 and 14–18 of the hospitals, respectively, for 5 years. Bone metastasis was investigated using bone scintigraphy in only 5–7 % (data not shown).