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Endoscopic mucosal resection (EMR) of early gastric cancer (EGC) has developed in the early 1980s, such as strip biopsy method [1], endoscopic resection with local injection of hypersaline-epinephrine (ERHSE) method [2], endoscopic mucosal resection with a cap-fitted panendoscope (EMRC) method [3], endoscopic aspiration mucosectomy (EAM) method [4], and EMR with a ligating device (EMR-L) method [5]. These methods are classified into conventional EMR methods. These are simple and safe methods, but lesion size which can be resected in en bloc fashion is limited.

Endoscopic submucosal dissection (ESD), which is characterized by mucosal incision surrounding a lesion followed by submucosal dissection, has developed in the late 1990s. This new type of methods such as IT knife method [6], hook knife method [7], and flex knife method [8] resulted in extending indications for safe and large en bloc resection.

Indications for EMR/ESD of EGC were proposed by the Japanese gastric cancer treatment guidelines of the Japanese Gastric Cancer Association (JGCA) [9] based on published analysis of a large clinicopathological database combining surgical cases of EGCs obtained from two large Japanese cancer centers [10].

1.1 Absolute Indication for EMR/ESD (Endoscopic Resection as a Standard Treatment)

The principle behind indications for EMR/ESD is EGC which has negligible risk of lymph node metastasis and is suitable for en bloc resection. Therefore, the absolute

Table 1.1 Endoscopic mucosal resection (EMR) indication

Principles of indication	Tumor with little possibility of lymph node metastasis, which can be removed en bloc according to its location and size
Criteria details	Macroscopic mucosal cancer (cM) of differentiated type (pap, tub1, tub2) less than 2 cm in diameter No ulceration or scar in cases of depressed type, irrespective of macroscopic type

indication for EMR/ESD is defined as an EGC which is a differentiated-type adenocarcinoma without ulcerative findings (UL(-)) and of which the depth of invasion is clinically diagnosed as T1a and the diameter is ≤ 2 cm. The necessary conditions for curative resection are lesions which can be resected en bloc, with tumor size ≤ 2 cm, adenocarcinoma of differentiated type, pT1a, horizontal/vertical margins negative, and without lymphatic or vascular involvements (Table 1.1).

1.2 Expanded Indications for ESD (Endoscopic Resection as an Investigative Treatment)

A previous report containing analyses of long-term prognosis of large number of patients with EGCs demonstrated that the 5-year cancer-specific survival rates of EGC limited to the mucosa or the submucosa were 99 % and 96 %, respectively [11]. Therefore, allowable risks of lymph node metastases for ESD of EGCs which are limited to the mucosa or the submucosa are less than 1 % and 4 %, respectively. The gastric cancer treatment guidelines of the JGCA [9] proposed three categories for expanded criteria for ESD: (1) intramucosal differentiated-type cancers (cT1a) >2 cm without ulcer findings, (2) intramucosal differentiated-type cancers (cT1a) ≤ 3 cm with ulcer findings, and (3) intramucosal undifferentiated-type cancers (cT1a) ≤ 2 cm without ulcer

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Tissue-type	Invasion depth	Intramucosal cancer				Minute Submucosal Cancer	
		UL (-)		UL (+)		≤SM1	SM1<
		≤20 mm	20 mm <	≤30 mm	30 mm <	≤30 mm	Any size
Well differentiated adenocarcinoma (WDA)							
Poorly differentiated adenocarcinomas (PDAs)							

Absolute indication for EMR/ESD
 Expanded indications for ESD
 Possible expansion for ESD
 "out of indications" for EMR/ESD

Fig. 1.1 Absolute indication for EMR/ESD and expanded indications for ESD

Table 1.2 Criteria for expansion of local treatment, derived from our results

Criteria	Intramucosal cancer	Intramucosal cancer	Minute submucosal penetration (SM1)	Undifferentiated intramucosal cancer
	Differentiated adenocarcinoma	Differentiated adenocarcinoma	Differentiated adenocarcinoma	
	No lymphovascular invasion	No lymphovascular invasion	No lymphovascular invasion	No lymphovascular invasion
	Irrespective of ulcer findings	Without ulcer findings		Without ulcer findings
	Tumor less than 3 cm in size	Irrespective of tumor size	Tumor less than 3 cm in size	Tumor less than 3 cm in size
Incidence	1/1230 (0 %)	0/929 (0 %)	0/145 (0 %)	0/141 (0 %)
95 % CI	0–0.3 %	0–0.4 %	0–2.5 %	0–2.6 %

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findings. The necessary conditions for curative resection are defined as below: (a) en bloc, tumor size >2 cm, differentiated type, pT1a, and without ulcer findings; (b) en bloc, tumor size ≤3 cm, differentiated type, pT1a, and with ulcer findings; (c) en bloc, tumor size ≤2 cm, undifferentiated type, pT1a, and without ulcer findings; and (d) en bloc, tumor size ≤3 cm, differentiated type, and pT1b (SM < 500 μm). Horizontal/vertical margins negative and no lymphatic or vascular involvements are common conditions in all categories (Fig. 1.1, Table 1.2).

Evidences concerning mixed histological types with differentiated- and undifferentiated-type gastric cancers are still insufficient. Therefore, conditions as below are considered as indications for additional surgical resection with lymph node dissection: (i) areas of undifferentiated-type carcinoma that exceed 2 cm in (a) above, (ii) any components of undifferentiated-type carcinoma in (b) above, and (iii) undifferentiated-type components in the submucosal invasion in (d) above.

1.3 Lesions Which Are “Out of Indications” for EMR/ESD (Endoscopic Resection in Special Situations)

Lesions which do not fulfill the absolute indication or the expanded indications are considered as “out-of-indication” lesions. Also, lesions which show lymphovascular invasions by histopathological evaluation are categorized as “out-of-indication” lesions.

“Out-of-indication” lesions, in general, are estimated to have risks of lymphatic invasion of at least 5–10 % and therefore are recommended for surgical resection by the gastric cancer treatment guidelines of the JGCA [9]. However, endoscopic resection may be considered as an alternative treatment in situations when surgical treatments are difficult because of old age or higher risk of complications.

1.4 Curative and Non-curative Resections

Curability status must be determined finally by pathological evaluations of endoscopically resected specimens. Pathologically speaking, complete curability must fulfill all of the abovementioned conditions of expanded indications as well as confirmation of cancer-free cut ends and absence of lymphatic and vascular invasions. Since divided resections make evaluation for cut ends, as well as depth of invasion, and lymphovascular involvements very difficult, en bloc resections are desirable. Even when pre-resection diagnosis based on biopsy is WDA, resection is non-curative if the final pathological diagnosis is undifferentiated adenocarcinomas. When ulcer scars are not detectible endoscopically but confirmed histologically, curability status must be considered as in ulcer-accompanied lesions.

1.5 Future Perspectives of ESD

There are a few reports about long-term prognosis about expanded criteria for ESD. Gotoda et al. reported that the 5-year overall survival of the expanded criteria group ($n = 625$) was 93.4 % and there was no significant difference with guideline criteria group ($n = 635$, 92.4 %) [12]. Multi-center prospective studies of expanded criteria for ESD were ongoing and final results were desired for more reliable evidences [13, 14]. The behavior of mixed-type EGCs is unclear. Takizawa et al. reported that a mixed type with a predominantly undifferentiated component should be managed the same way as a differentiated type. Further investigation is required to manage mixed-type EGCs [15].

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