

Guidelines

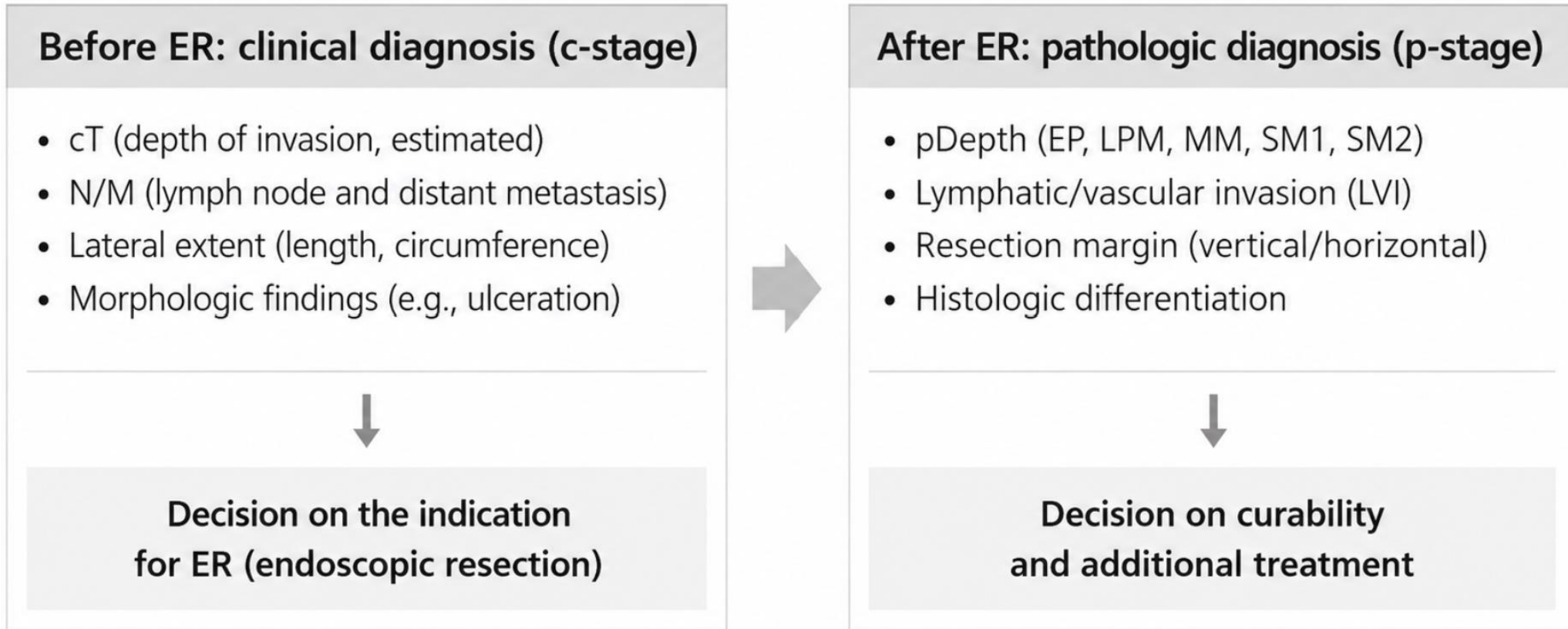
Endoscopic submucosal dissection/endoscopic mucosal resection guidelines for esophageal cancer

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Part 1. ESCC

Clinical staging $\neq$ Pathologic curability



ESCC: invasion depth / Endoscopic resection 전략

Clinical/Pathological Category	Depth of Invasion	Key Clinical Implication	5-Year Cumulative Metastasis Rate After ER
EP / LPM	Epithelium / Lamina propria mucosae	Very low risk of lymph node metastasis → ER strongly considered	0.4%
MM	Muscularis mucosae	Intermediate risk; ER may be considered as initial treatment for cMM	8.7%
SM1	Submucosal invasion ≤200 μm (ER specimen)	ER weakly recommended for non-circumferential cSM1, N0M0	7.7%
SM2	Submucosal invasion >200 μm (ER specimen)	Additional treatment strongly recommended if confirmed pathologically	36.2%

CQ1 | ER as first-line treatment for cMM/SM1 ESCC

Recommendation: Endoscopic resection is weakly recommended **as first-line treatment for preoperatively diagnosed cT1a-MM/T1b-SM1 non-circumferential esophageal squamous cell carcinoma**. Strength of evidence: C

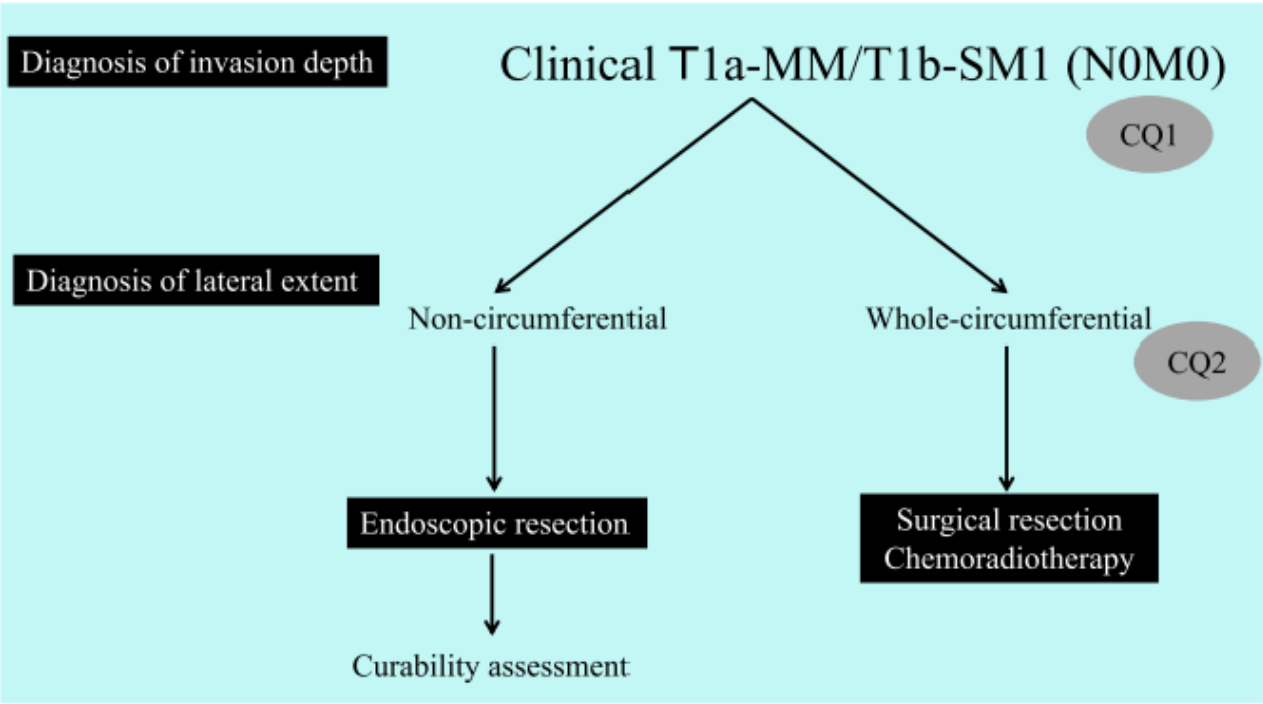
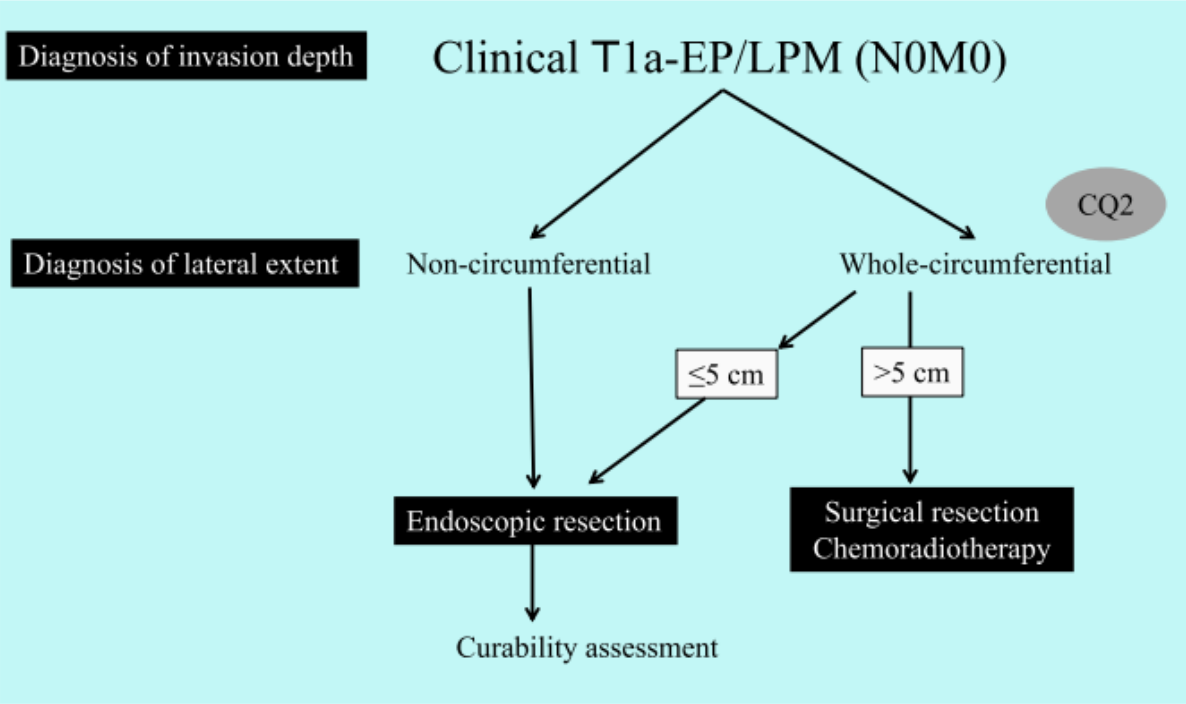
① cMM/SM1 술전 진단은 부정확 → 최종 병리 분포

Pre-ER 진단 : cMM/SM1	pEP/LPM	pMM/SM1	pSM2
Magnifying endoscopy (B2 vessel, n=212)	27.4%	55.7%	17.0%
NBI IPCL V3 (Sato 2015)	29.8%	42.3%	27.9%
EUS (n=58)	55.2%	29.3%	15.5%

pEP/LPM 27.4-55.2% → ER 만으로 근치 가능
pSM2 15.5-27.9% → ER 후 추가 치료 필요

② ER vs 수술 (pT1 ESCC, 후향 단일기관 2 건)

Shanghai (Zhang 2019)	ESD	Surgery	P
Severe complications	15.2%	27.7%	<0.001
Esophageal fistula	0.3%	16.4%	<0.001
Post-treatment stenosis	13.4%	9.9%	NS
Procedure time / stay	49 min / 3 d	240 min / 11 d	<0.001
OS · DSS · metastasis (mean 21 mo)	차이 없음 (교란인자 보정 후에도 유사)		
Korea PSM (Min 2018) mean 43 vs 63 mo	OS · DSS · RFS 차이 없음		



JCOG0508: Pathology-guided additional treatment after ER

Pathological findings after ER	Subsequent strategy
pMM, vascular invasion (–), margin (–)	Observation
pMM, vascular invasion (+) or pSM, margin (–)	Prophylactic CRT (41.4 Gy)
Positive resection margin	Definitive CRT

3-year OS

92.6% (90% CI 88.5–95.2)

3-year PFS

89.7% (90% CI 84.2–93.4)

Key additional findings

- Group size: A 74, B 87, C 15
- Among 15 patients with recurrence or metastasis, 7 underwent salvage surgery, and 2 survived. (p=0.477)
- Prophylactic CRT group: 3-year OS 90.7%; ER-related grade ≥3 stenosis: 0.6%

CQ2 |Whole-circumferential lesions

Recommendation: Endoscopic resection is weakly recommended for **cT1a-EP/LPM superficial squamous cell carcinomas with a major axis length ≤50mm and involving the entire circumference of the esophagus**, upon implementing preventive measures for stenosis Strength of evidence: C

Without prophylaxis		With steroid prophylaxis		
Stenosis	Mean balloon dilations	Injection	Oral	Both
100% (31/31)	26 sessions	76% (45명)	55% (44명)	71% (14명)

Resection length (major axis)	≥6 balloon dilations required
>50 mm	85% (11/13)
≤50 mm	17% (1/6)

CQ3 | Traction-assisted ESD

Recommendation: Use of a traction device using a clip and thread is weakly recommended when performing ESD for superficial esophageal squamous cell carcinoma. Strength of evidence: B

Table 5 Procedure time

Clip and thread	With	Without	<i>P</i> -value	Reference
Procedure time (min)	19.8	31.8	0.044	2
	104	156	0.003	3
	27.5	34.8	0.252	4

CQ4 | Prevention of post-ESD stenosis

Recommendation: Local injection of triamcinolone is weakly recommended when mucosal defects affecting $\geq 3/4$ of the esophageal circumference occur after endoscopic resection for superficial esophageal squamous cell carcinoma. Strength of evidence: B

Non-circumferential defects		
Degree of mucosal defect	Stenosis rate (%) TA vs control	No. of dilation sessions
>2/3	45 vs 82	6.1 vs 12.5
>3/4	36 vs 61	2 vs –
>3/4	10 vs 66	0 vs 2
>3/4	19 vs 75	1.7 vs 6.6

Whole-circumferential defects		
Injection dose (mg)	Stenosis rate (%) TA vs control	No. of dilation sessions
40	100 vs 100	10.4 vs 22.2
50	100 vs 100	6.0 vs 12.5

- Triamcinolone reduces stenosis in non-circumferential defects (10–45% vs 61–82%).
- In whole-circumferential defects, stenosis remained 100% despite triamcinolone, although the number of dilation sessions decreased (6–10.4 vs 12.5–22.2).

CQ5 | Is routine PPI necessary?

Recommendation: It is weakly recommended that **PPIs should not be administered to prevent bleeding and promote ulcer healing following endoscopic resection for superficial esophageal squamous cell carcinoma**, except in patients with GERD symptoms or reflux esophagitis of Los Angeles grade A or higher at the time of endoscopic resection. Strength of evidence: C

Ulcer healing after ER (RCT)

No PPI
84%
(ulcer healing)

PPI
85%
(ulcer healing)

No significant benefit with routine PPI.

PPI use in GERD/reflux esophagitis

GERD symptoms
25% (baseline prevalence)

Reflux esophagitis (LA grade A or higher)
30% (baseline prevalence)



Consider PPI in patients with GERD symptoms or reflux esophagitis (LA grade $\geq$ A) at the time of ER.

CQ6 | pMM, vascular invasion negative

Recommendation: No recommendation could be determined for or against additional surgery or CRT after ER for pT1a-MM ESCC with negative vascular invasion. Strength of evidence: D

Metastasis rate in pMM, vascular invasion negative	
Study (Reference)	Metastasis rate n/N (%)
Ref. 3	0/42 (0%)
Ref. 4	1/6 (16.7%)
Ref. 5	2/21 (9.5%)
Ref. 6	1/55 (1.8%)
Ref. 7	2/24 (8.3%)

Metastasis rate by additional treatment (pMM)			
Vascular invasion	Follow-up n/N (%)	Additional surgery n/N (%)	Additional CRT n/N (%)
Negative	12/216 (5.6%)	0/6 (0%)	1/17 (5.9%)
Positive	3/14 (21.4%)	1/20 (5.0%)	7/45 (15.6%)

- Key points**
- pMM with negative vascular invasion showed a low metastasis rate in observational studies (e.g., 5.6%, 12/216).
 - Additional surgery or CRT after ER did not show a clear reduction in metastasis, and the evidence is limited and inconsistent.

Endoscopic resection

Histological
diagnosis

pT1a-EP/LPM
ly(-), v(-)

Follow-up

pT1a-MM
ly(-), v(-)

Comprehensive evaluation
of the need
for additional treatment

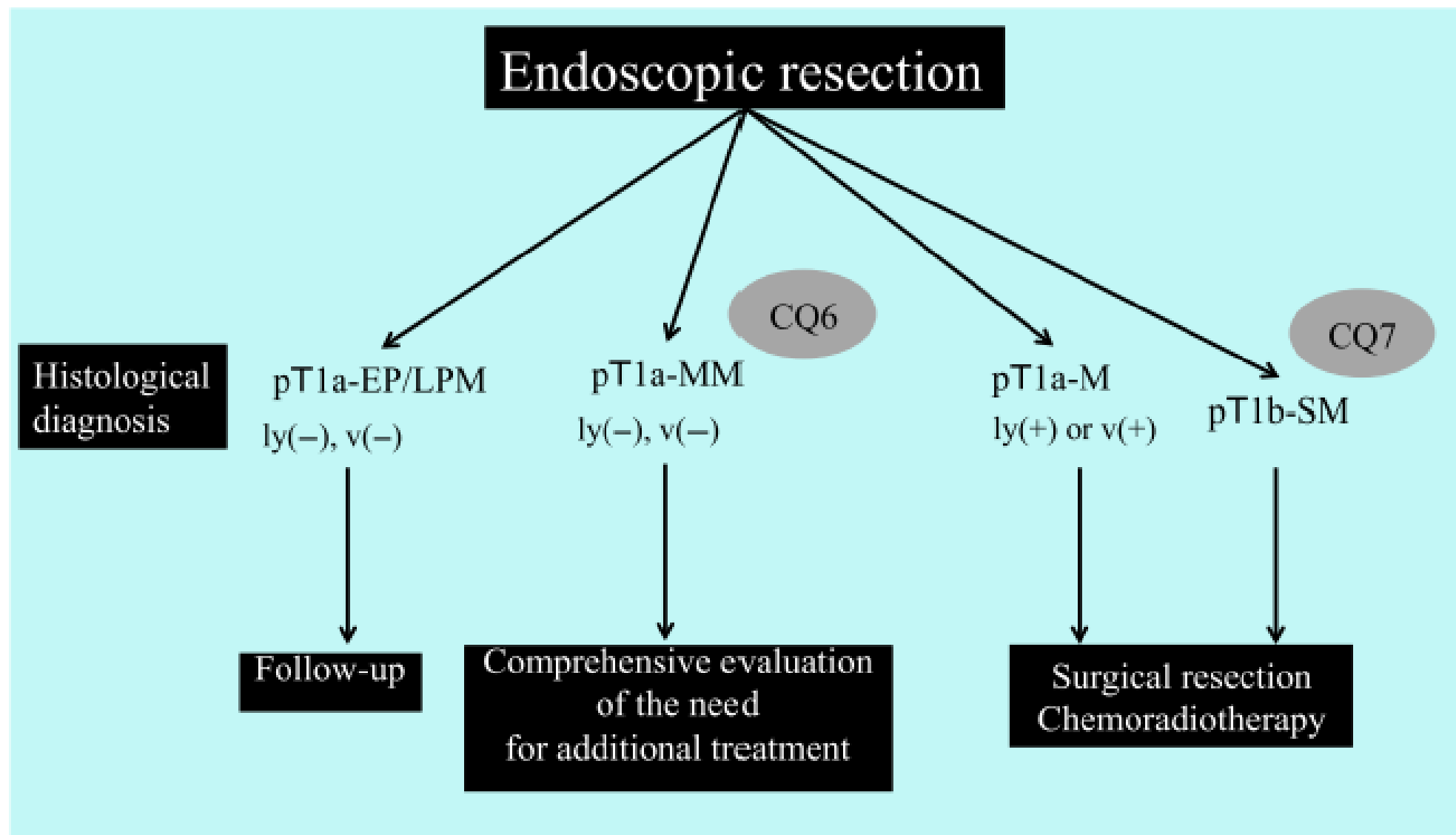
CQ6

pT1a-M
ly(+) or v(+)

Surgical resection
Chemoradiotherapy

CQ7

pT1b-SM



CQ7 | pT1b-SM: additional treatment

Recommendation: Additional surgical resection or CRT is strongly recommended after ER for pT1b-SM ESCC.Strength of evidence: D

Table 11 Summary of metastasis in patient groups according to the presence or absence of vascular invasion in pSM1/2 cancer

Invasion depth	Vascular invasion	Metastasis rate		
		Follow-up observation group	Additional surgical resection group	Additional chemoradiotherapy group
pSM1	Negative	13.2% (5/38 patients)	0% (0/5 patients)	2.9% (1/35 patients)
pSM2	Negative	18.8% (3/16 patients)	8.3% (1/12 patients)	9.3% (8/86 patients)
pSM1	Positive	60.0% (3/5 patients)	0% (0/14 patients)	17.9% (5/28 patients)
pSM2	Positive	0% (0/4 patients)	0% (0/21 patients)	28.1% (23/82 patients)

Key points

- In pSM1/SM2 with vascular invasion (–), the metastasis rate was 14.8% with surveillance, compared with 5.9% after surgery and 7.4% after CRT.
- In pSM1/SM2 with vascular invasion (+), the metastasis rate was 33.3% with surveillance.

CQ8-9 | Risk reduction and endoscopic surveillance

CQ8 | Alcohol and smoking abstinence

Recommendation

Abstinence from alcohol and smoking is strongly recommended after endoscopic resection of superficial esophageal squamous cell carcinoma.

Strength of evidence: B

Key evidence

- Alcohol abstinence: prospective cohort (Katada, n=331) reported lower metachronous ESCC risk, HR 0.47 (95% CI 0.25–0.91); multiple Lugol-voiding lesions HR 0.23 (0.09–0.60).
- Smoking cessation: metachronous ESCC HR 0.47 (95% CI 0.26–0.91) in the same cohort; a registry of 29,795 cancer survivors reported HR 0.49 (0.28–0.86).
- Observational evidence; survival benefit has not been established.

CQ9 | Endoscopic interval: metachronous ESCC

Recommendation

Endoscopic examination at least once a year is strongly recommended for surveillance following ER for superficial ESCC.

Strength of evidence: C

Key evidence

- Annual incidence of metachronous esophageal cancer was approximately 2.2–9.0% across cited studies.
- Reported surveillance intervals included 6 months (3 studies), 12 months (2), and 6–12 months (1); most metachronous cancers remained endoscopically treatable.
- Multiple Lugol-voiding lesions indicate higher metachronous cancer risk and may warrant closer follow-up.

CQ10-11 | Other organs and metastasis surveillance

CQ10 | Metachronous cancers in other organs

Recommendation

Surveillance for metachronous cancers in other organs using upper GI endoscopy is strongly recommended following ER for superficial ESCC.

Strength of evidence: C

Key evidence

- Head and neck cancer risk is markedly elevated (SIR 6.7–20.1). Increased lung cancer risk was also reported.
- Head and neck cancer detection by number of Lugol-voiding lesions (none / 1–9 / ≥ 10): 0% / 1.7% / 8.6%.
- NBI outperformed white-light observation in cited head and neck cancer studies (9.8% vs 3.9%; 10.9% vs 1.2%).

CQ11 | CT for metastasis (pMM or deeper)

Recommendation

CT imaging at least once a year is weakly recommended for surveillance of metastasis after ER for superficial ESCC with pMM or deeper invasion.

Strength of evidence: C

Key evidence

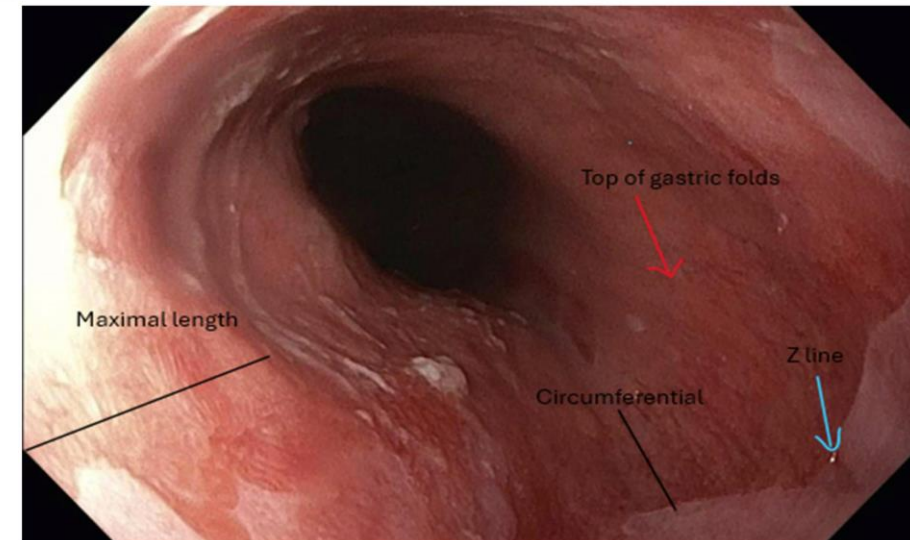
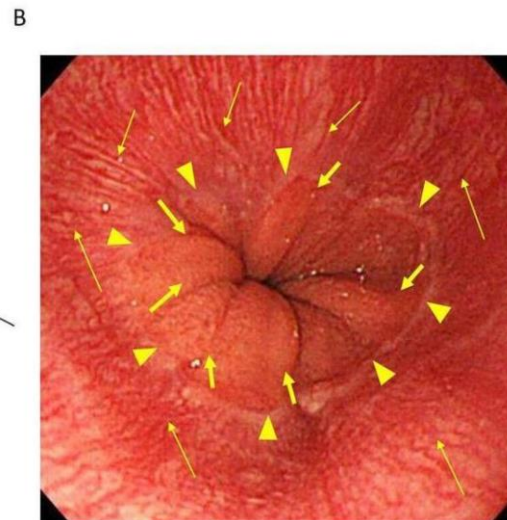
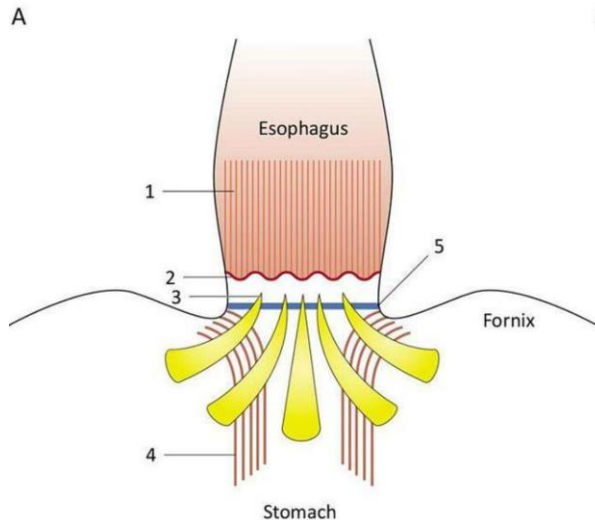
- 5-year cumulative metastasis after ER (n=402): pEP/LPM 0.4%; pMM 8.7%; pSM1 7.7%; pSM2 36.2%.
- JCOG0508 (n=176) used CT every 4 months for 3 years, then every 6 months; recurrence/metastasis occurred in 15 patients (8.7%).
- No study established that earlier detection improves overall survival; endoscopy and CT address different surveillance targets.

Part 2. Barrett-associated Adenocarcinoma

Barrett-associated Adenocarcinoma: Definition

Issue	Japan	Western countries
EGJ definition	Distal end of esophageal palisade vessels	Proximal end of gastric folds
Intestinal metaplasia	Not required	Required (except UK)
Long-segment Barrett	Circumferential Barrett mucosa ≥ 3 cm (LSBE-C)	Maximum length ≥ 3 cm (LSBE-M)
Short-segment Barrett	Circumferential Barrett mucosa < 3 cm (SSBE-C)	Maximum length < 3 cm (SSBE-M)

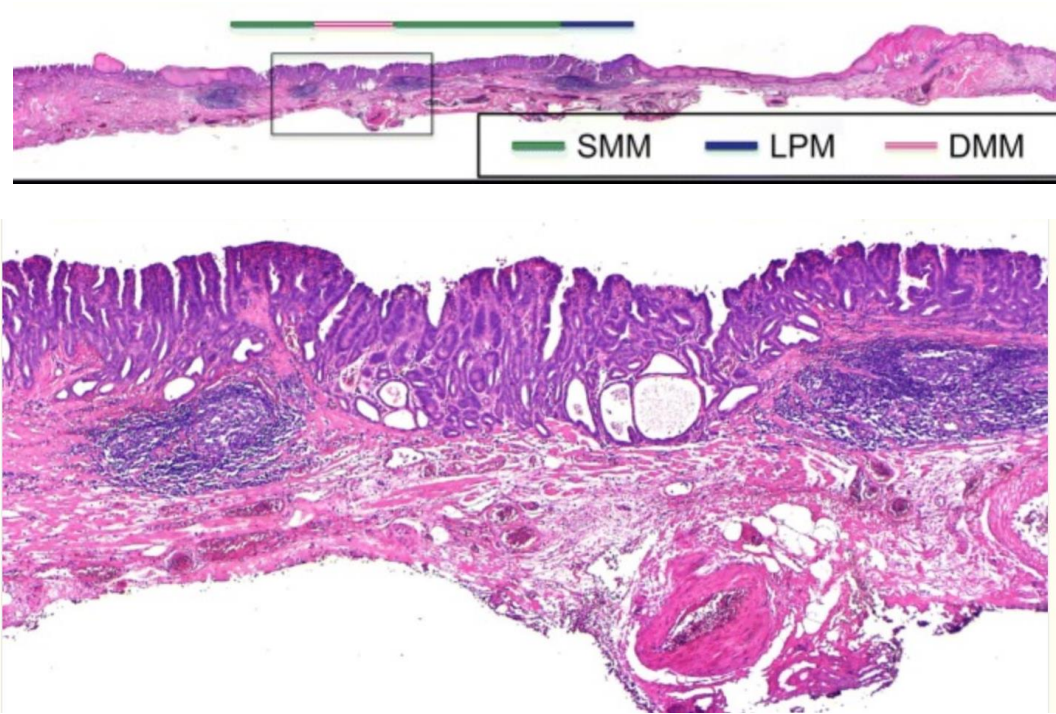
Why Barrett differs from ESCC	
Issue	Barrett-associated EAC
Clinical staging	EUS not routinely recommended for superficial EAC
Lateral mapping	NBI magnification $\pm$ acetic acid; assess subsquamous extension
Mucosal anatomy	Duplicated MM: SMM / DMM
Post-ER factors	pDMM, differentiation, LVI, R0



Barrett pathology: duplicated muscularismucosae

Layer (superficial → deep)	Clinical meaning
Surface epithelium / lamina propria	T1a
Superficial muscularis mucosae (SMM)	T1a
Between SMM and DMM	Still mucosa: T1a
Deep muscularis mucosae (DMM)	Still T1a; CQ16 focuses here
True submucosa	T1b; different lymph-node risk

DMM invasion ≠ submucosal invasion | avoid overstaging



CQ12–13 | Pre-ER lateral extent assessment in Barrett EAC

CQ12 | Magnifying image-enhanced endoscopy

Recommendation: Image-enhanced magnifying endoscopy is weakly recommended to delineate lateral extent before ER for superficial esophageal adenocarcinoma. Strength of evidence: D

Key evidence

- ESD series: R0 resection 74.5%; among 134 R1 lesions, 54 (40.3%) had positive horizontal margins.
- Magnifying NBI studies reported sensitivity and specificity around 94% for detecting HGD/adenocarcinoma.

Table 1b. Diagnostic performance by magnifying endoscopy with NBI

Target lesion (n)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Reference
HGD (41) Mucosal pattern diagnosis	100	98.8	99.0	8
HGD (36) Vascular pattern diagnosis	100	97.4	98.2	8
HGD (8)	100	100	-	9
Adenocarcinoma (6)	100	100	100	10
HGD (32)	96.2	98.7	98.5	11
HGD (91) HGD (1) Adenocarcinoma (4)	100	97.4	97.7	12
HGD (28) Adenocarcinoma (31)	91.1	92.9	92.2	20
HGD (8) Adenocarcinoma (63)	93.1	96.2	95.3	17

HGD, high-grade dysplasia; IGD, low-grade dysplasia; NBI, narrow-band imaging.

CQ13 | Biopsy surrounding LSBE mucosa

Recommendation: Biopsies from surrounding mucosa are weakly recommended to assess lateral extent before ER for adenocarcinoma arising in LSBE (maximum length ≥3 cm). Strength of evidence: D

Key evidence

- R0 resection in one European series: 85% in SSBE vs 48% in LSBE (HGD lesions).
- Japanese ESD series: R0 resection 91% in SSBE vs 70% in LSBE.

CQ14 | Routine EUS for invasion depth?

Recommendation: Routine EUS for invasion-depth diagnosis before ER of superficial esophageal adenocarcinoma is **weakly discouraged**. Strength of evidence: C

Comparison	Accuracy
White-light macroscopic assessment	83.4%
EUS (same prospective study)	79.6%
Published EUS T1a/T1b discrimination (six studies)	76.4–85.4%
Japanese Barrett EAC study	73%; T1a sensitivity 56%

Overstaging 가능성 + WLI보다 명확한 추가 이득 없음 → routine EUS 비권고

CQ15 | ESD versus EMR

Recommendation: **ESD is strongly recommended** over EMR for radical resection of superficial esophageal adenocarcinoma suitable for endoscopic treatment. Strength of evidence: B

Outcome	EMR	ESD
En bloc resection	50.0%	96.4%
R0 resection	39.7%	81.9%
Local recurrence	12.4%	2.5%
All procedure-related AEs	9.3%	10.5%
Perforation	0.4%	1.5%

CQ16 | Differentiated pDMM after R0 ER

Recommendation: Additional surgery is weakly discouraged for differentiated pDMM adenocarcinoma after R0 ER when vascular invasion and poorly differentiated components are absent. Strength of evidence: C

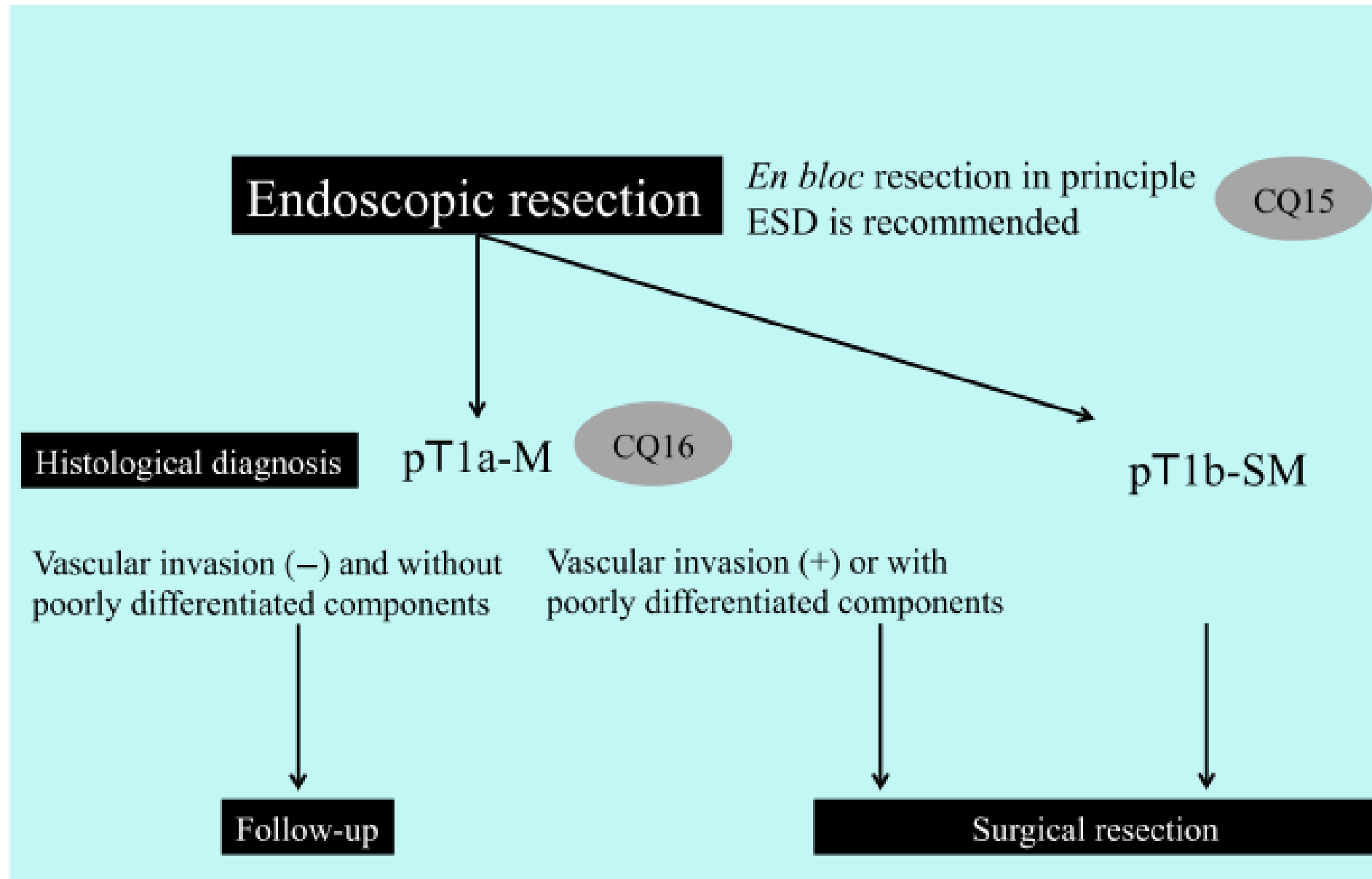
Eligibility after ER

pDMM invasion	Intramucosal (T1a)
Differentiated histology	No poorly differentiated component
Vascular invasion	Negative
Resection margin	R0

Observed lymph-node metastasis

0 / 105	Surgical specimens
1 / 200	ER cases (0.5%)

Take-home: pDMM invasion alone does not mandate esophagectomy when differentiated, LVI-negative, and R0.



CQ17-18 | Post-ER surveillance of Barrett EAC

CQ17 | Endoscopy interval after ER

Endoscopy **approximately once a year** is weakly recommended after ER of superficial EAC arising in LSBE (maximum length ≥ 3 cm). Strength of evidence: C.

Endoscopy interval by segment length

Segment	Key data (annual incidence)	Recommended interval
LSBE ≥ 3 cm	Post-ER (LSBE-C): 0.70% No prior cancer: ~1% (West 0.91%, Japan 1.2%)	~Annual (CQ17)
SSBE <3 cm	Post-ER (SSBE-C): 0.29% No prior cancer (West): 0.29%	Not established (2–3 years discussed)

CQ18 | Image-enhanced and magnifying endoscopy

Image-enhanced endoscopy and **magnifying endoscopy** are weakly recommended for surveillance following ER of superficial esophageal adenocarcinoma. Strength of evidence: C.

Diagnostic accuracy for detecting dysplasia or cancer

Modality	Sensitivity (%)	Specificity (%)
NBI (magnifying > non-magnifying)	94 (83–98)	94 (81–99)
Acetic acid (1–3%) + magnification	92 (83–97)	96 (85–99)
AFI · indigo carmine · methylene blue · pCLE	Low sensitivity and/or specificity → not recommended	