See "Clinical practice guideline for endoscopic resection of early gastrointestinal cancer" on page 127-157.

Supplementary Material 1. PICOs for Each Statement

1. Description of PICOs for Superficial Esophageal Squamous Cell Carcinoma

Statement E1: We recommend endoscopic resection for SESCC without distant or lymph node metastasis, excluding those with obvious submucosal invasion. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. What are the indications for endoscopic resection of superficial esophageal squamous cell carcinoma?

Patient: Patients who undergo either endoscopic resection or esophagectomy for superficial esophageal squamous cell carcinoma without lymph node metastasis
Intervention: Endoscopic resection
Comparator: Esophagectomy
Outcome: Survival rate
Study design: Randomized controlled trial (RCT) or non-RCT

Statement E2: We recommend Lugol chromoendoscopy and/or image-enhanced endoscopy to define the extent of lesion before endoscopic treatment of SESCC. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Does chromoendoscopy or image-enhanced endoscopy before endoscopic resection of superficial esophageal squamous cell carcinoma help the evaluation of the lateral margin of the lesion?

Patient: Patients who were diagnosed with superficial esophageal squamous cell carcinoma
Intervention: Chromoendoscopy, image-enhanced endoscopy
Comparator: No chromoendoscopy or image-enhanced endoscopy after diagnosis of superficial esophageal squamous cell carcinoma
Outcome: Lateral margin
Study design: RCT or non-RCT

Statement E3: We recommend endoscopic ultrasound to define the stage of SESCC before endoscopic treatment. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Does endoscopic ultrasound (EUS) before endoscopic resection of superficial esophageal squamous cell carcinoma help to stage the disease?

Patient: Patients who were diagnosed with superficial esophageal squamous cell carcinoma
Intervention: EUS
Comparator: No EUS after diagnosis of superficial esophageal squamous cell carcinoma
Outcome: Depth of invasion, lymph node metastasis
Study design: RCT or non-RCT

Statement E4: We suggest magnifying endoscopy with narrow band imaging for SESCC to assess the depth of invasion before endoscopic treatment. (Grade of recommendation: weak, Level of evidence: low)

Q1. Does magnifying endoscopy with narrow band imaging (MENBI) before endoscopic resection of superficial esophageal squamous cell carcinoma help the evaluation of the depth of invasion?

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Patient: Patients who were diagnosed with superficial esophageal squamous cell carcinoma
Intervention: MENBI
Comparator: No MENBI after diagnosis of superficial esophageal squamous cell carcinoma
Outcome: Depth of invasion
Study design: RCT or non-RCT

Statement E5: We recommend endoscopic submucosal dissection rather than endoscopic mucosal resection for en bloc and curative resection of SESCC confined to the mucosa. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Is ESD more effective than EMR in patients with superficial esophageal squamous cell carcinoma in terms of en bloc resection, R0 resection and curative resection?

Patient: Patients who undergo endoscopic resection for superficial esophageal squamous cell carcinoma
Intervention: Endoscopic submucosal dissection
Comparator: Endoscopic mucosal resection
Outcome: en bloc resection, R0 resection, curative resection
Study design: RCT or non-RCT

Statement E6: We recommend oral steroid or local steroid injection therapy for patients who develop mucosal defects in >75% of the esophageal circumference after endoscopic submucosal dissection to prevent esophageal stricture. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Is steroid administration needed after endoscopic resection in patients with superficial esophageal squamous cell carcinoma to decrease the risk of stenosis?

Patient: Patients who undergo endoscopic resection for superficial esophageal squamous cell carcinoma
Intervention: Steroid administration after endoscopic resection (oral administration or local injection)
Comparator: No steroid administration after endoscopic resection
Outcome: Stenosis rate, number of endoscopic dilatation, adverse event
Study design: RCT or non-RCT

Statement E7: No additional treatment is recommended after en bloc complete resection of SESCC invading no more than the lamina propria with no lymphovascular invasion because of a very low risk of lymph node metastasis. (Grade of recommendation: strong, Level of evidence: moderate) As the risk of lymph node metastasis of a tumor invading into the muscularis mucosa without lymphovascular invasion is low, a close follow-up after en bloc complete endoscopic resection can be considered without additional treatment. (Grade of recommendation: weak, Level of evidence: low) In case of a tumor with submucosal invasion, lymphovascular invasion, and/or positive vertical resection margin, additional treatment is recommended. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Is there a difference between observation without surgery and rescue surgery in terms of recurrence and survival in patients who achieve R0 resection by endoscopic resection for mucosal esophageal squamous cell carcinoma without lymphovascular invasion?

Patient: Patients who achieve R0 resection by endoscopic resection for mucosal esophageal squamous cell carcinoma without lymphovascular invasion
Intervention: Observation
Comparator: Rescue (additional) surgery
Outcome: Recurrence and survival rates
Study design: RCT or non-RCT

2. Description of PICOs for Early Gastric Cancer

Statement G1: We recommend chromoendoscopy/image-enhanced endoscopy to determine the extent of lesion before endoscopic treatment of early gastric cancer (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Does chromoendoscopy or image-enhanced endoscopy before endoscopic resection of early gastric cancer help the evaluation of the lateral margin of the lesion?

Patient: Patients who were diagnosed with early gastric cancer
Intervention: Chromoendoscopy, image-enhanced endoscopy
Comparator: No chromoendoscopy or image-enhanced endoscopy after diagnosis of early gastric cancer
Outcome: Lateral margin
Study design: RCT or non-RCT

Statement G2: Endoscopic ultrasonography before endoscopic resection of early gastric cancer may be helpful in determining the depth of invasion in some patients with early gastric cancer. (Grade of recommendation: weak, Level of evidence: moderate)

Q1. Does EUS before endoscopic resection of early gastric cancer help the evaluation of the depth of invasion?

Patient: Patients who were diagnosed with early gastric cancer
Intervention: EUS
Comparator: No EUS after diagnosis of early gastric cancer
Outcome: Depth of invasion
Study design: RCT or non-RCT

Statement G3: We recommend endoscopic resection for early gastric cancer of well or moderately differentiated tubular or papillary adenocarcinoma meeting endoscopically estimated tumor size ≤ 2 cm and endoscopically suspected mucosal cancer without ulcer. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Can we recommend endoscopic resection for early gastric cancer of well or moderately differentiated tubular or papillary adenocarcinoma meeting endoscopically estimated tumor size ≤ 2 cm and endoscopically suspected mucosal cancer without ulcer?

Patient: Patients with early gastric cancer of well or moderately differentiated tubular or papillary adenocarcinoma meeting endoscopically estimated tumor size ≤ 2 cm and endoscopically suspected mucosal cancer without ulcer
Intervention: Endoscopic resection
Comparator: Gastrectomy with lymph node dissection
Outcome: Survival rate
Study design: RCT or non-RCT

Statement G4: We suggest endoscopic resection for early gastric cancer of well or moderately differentiated tubular or papillary adenocarcinoma with the following endoscopic findings: 1) mucosal cancer > 2 cm without ulcer, or 2) mucosal cancer ≤ 3 cm with ulcer. (Grade of recommendation: weak, Level of evidence: moderate)

Q1. Can we suggest endoscopic resection for early gastric cancer of well or moderately differentiated tubular or papillary adenocarcinoma with the following endoscopic findings: 1) mucosal cancer > 2 cm without ulcer, or 2) mucosal cancer ≤ 3 cm with ulcer?

Patient: Patients with early gastric cancer of well or moderately differentiated tubular or papillary adenocarcinoma with the following endoscopic findings: 1) mucosal cancer > 2 cm without ulcer, or 2) mucosal cancer ≤ 3 cm with ulcer
Intervention: Endoscopic resection
Comparator: Gastrectomy with lymph node dissection
Outcome: Survival rate
Study design: RCT or non-RCT

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Statement G5: We suggest endoscopic resection for poorly differentiated tubular adenocarcinoma, poorly cohesive carcinoma, or signet ring cell carcinoma meeting the following endoscopic findings: endoscopically estimated tumor size ≤2 cm, endoscopically mucosal cancer, and no ulcer in the tumor (Grade of recommendation: weak, Level of evidence: low)

Q1. Can we suggest endoscopic resection for poorly differentiated tubular adenocarcinoma, poorly cohesive carcinoma, or signet ring cell carcinoma meeting the following endoscopic findings: endoscopically estimated tumor size ≤2 cm, endoscopically mucosal cancer, and no ulcer in the tumor?

Patient: Patients with early gastric cancer of poorly differentiated tubular adenocarcinoma, poorly cohesive carcinoma, or signet ring cell carcinoma meeting the following endoscopic findings: endoscopically estimated tumor size ≤2 cm, endoscopically mucosal cancer, and no ulcer in the tumor

Intervention: Endoscopic resection

Comparator: Gastrectomy with lymph node dissection

Outcome: Survival rate

Study design: RCT or non-RCT

Statement G6: We recommend prophylactic hemostasis of visible vessels on the post-resection ulcer caused by endoscopic resection of early gastric cancer to lower the risk of delayed bleeding (Grade of recommendation: strong, Level of evidence: low)

Q1. Can prophylactic hemostasis of visible vessels on the post-resection ulcer caused by endoscopic resection of early gastric cancer reduce the risk of delayed bleeding?

Patient: Patients who underwent endoscopic resection for early gastric cancer

Intervention: Prophylactic hemostasis of visible vessels on the post-resection ulcer

Comparator: No prophylactic hemostasis

Outcome: Delayed bleeding

Study design: RCT or non-RCT

Statement G7: We recommend proton pump inhibitors to decrease the risk of symptoms and complications associated with iatrogenic ulcers caused by endoscopic resection of early gastric cancer. (Grade of recommendation: strong, Level of evidence: high)

Q1. Can proton pump inhibitors decrease the risk of symptoms and complications associated with iatrogenic ulcers caused by endoscopic resection of early gastric cancer?

Patient: Patients who underwent endoscopic resection for early gastric cancer

Intervention: Use of proton pump inhibitors

Comparator: No use of proton pump inhibitors

Outcome: Symptoms and complications associated with iatrogenic ulcers

Study design: RCT or non-RCT

Statement G8: We recommend endoscopic closure as the first treatment option for perforation that occurred during endoscopic resection of early gastric cancer. (Grade of recommendation: strong, Level of evidence: low)

Q1. What is the first treatment option for perforation that occurred during endoscopic resection of early gastric cancer?

Patient: Patients with perforation that occurred during endoscopic resection

Intervention: Endoscopic closure

Comparator: Surgery or conservative management

Outcome: Closure rate

Study design: RCT or non-RCT

Statement G9: We recommend surgical gastrectomy if histopathological evaluation after endoscopic resection of early gastric cancer meets the criteria for non-curative resection. An exception applies if cancer invasion is observed at the horizontal resection margin only. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Is there a difference between observation without surgery and rescue surgery in terms of recurrence and survival in patients with early gastric cancer meeting the criteria for non-curative resection (an exception applies if cancer invasion is observed at the horizontal resection margin only)?

Patient: Patients with early gastric cancer meeting the criteria for non-curative resection (an exception applies if cancer invasion is observed at the horizontal resection margin only)
Intervention: Rescue surgery
Comparator: Observation without surgery
Outcome: Recurrence and survival
Study design: RCT or non-RCT

Statement G10: We recommend additional endoscopic management rather than surgical gastrectomy if histopathological evaluation of endoscopically resected early gastric cancer specimen shows positive involvement at the horizontal resection margin without any other findings compatible with non-curative resection. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Is there a difference between additional endoscopic therapy without surgery and rescue surgery in terms of recurrence and survival in patients with early gastric cancer with positive involvement at the horizontal resection margin without any other findings compatible with non-curative resection?

Patient: Patients with early gastric cancer with positive involvement at the horizontal resection margin without any other findings compatible with non-curative resection
Intervention: Additional endoscopic therapy
Comparator: Rescue surgery
Outcome: Recurrence and survival
Study design: RCT or non-RCT

Statement G11: We recommend *Helicobacter pylori* (*H. pylori*) eradication treatment after endoscopic resection of early gastric cancer in *H. pylori*-infected patients. (Grade of recommendation: strong, Level of evidence: high)

Q1. Can *Helicobacter pylori* eradication treatment after endoscopic resection of early gastric cancer reduce the metachronous gastric cancer in *H. pylori*-infected patients?

Patient: *H. pylori*-infected patients after endoscopic resection of early gastric cancer
Intervention: *Helicobacter pylori* eradication treatment
Comparator: No eradication
Outcome: Incidence of the metachronous gastric cancer
Study design: RCT or non-RCT

Statement G12: We recommend regular surveillance endoscopy every 6–12 months for patients who have had curative endoscopic resection of early gastric cancer based on absolute or expanded criteria for early detection of metachronous gastric cancer. (Grade of recommendation: strong, Level of evidence: low)

Q1. Does regular surveillance endoscopy every 6–12 months help the early detection of metachronous gastric cancer in patients who have had curative endoscopic resection of early gastric cancer based on absolute or expanded criteria?

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Patient: Patients who have had curative endoscopic resection of early gastric cancer based on absolute or expanded criteria
Intervention: Surveillance endoscopy every 6–12 months
Comparator: No surveillance endoscopy
Outcome: Early detection of metachronous gastric cancer
Study design: RCT or non-RCT

Statement G13: We suggest regular abdominopelvic computed tomography scan of 6- to 12-month interval for detection of extra-gastric recurrence after curative endoscopic resection of early gastric cancer based on absolute and expanded criteria. (Grade of recommendation: weak, Level of evidence: low)

Q1. Does regular abdominopelvic computed tomography scan every 6–12 months help the detection of extra-gastric recurrence in patients who have had curative endoscopic resection of early gastric cancer based on absolute or expanded criteria?

Patient: Patients who have had curative endoscopic resection of early gastric cancer based on absolute or expanded criteria
Intervention: Abdominopelvic computed tomography scan every 6–12 months
Comparator: No surveillance computed tomography scan
Outcome: Detection of extra-gastric recurrence
Study design: RCT or non-RCT

3. Description of PICOs for Early Colorectal Cancer

Statement C1: Poor histologic types (poorly differentiated adenocarcinoma, signet ring cell carcinoma, and mucinous carcinoma), deep submucosal invasion, lymphovascular invasion, and intermediate-to-high–grade tumor budding at the site of deepest invasion are risk factors of lymph node metastasis in early colorectal cancer. (Grade of recommendation: strong, Level of evidence: moderate

Q1. Does intramucosal colorectal cancer have the risk of lymph node metastasis?

Patient: Patients who were diagnosed with intramucosal colorectal cancer
Intervention: Not applicable
Comparator: Not applicable
Outcome: Incidence of lymph node metastasis
Study design: RCT or non-RCT

Q2. Is the risk of lymph node metastasis higher in the deep submucosal invasive colorectal cancer than in the superficial submucosal invasive colorectal cancer?

Patient: Patients who were diagnosed with submucosal colorectal cancer
Intervention: Patients who were diagnosed with deep submucosal colorectal cancer
Comparator: Patients who were diagnosed with superficial submucosal colorectal cancer
Outcome: Incidence of lymph node metastasis
Study design: RCT or non-RCT

Q3. Is the risk of lymph node metastasis higher in the submucosal invasive colorectal cancer with lymphovascular invasion than in the submucosal invasive colorectal cancer without lymphovascular invasion?

Patient: Patients who were diagnosed with submucosal colorectal cancer
Patient: Patients who were diagnosed with submucosal colorectal cancer with lymphovascular invasion
Comparator: Patients who were diagnosed with submucosal colorectal cancer without lymphovascular invasion
Outcome: Incidence of lymph node metastasis
Study design: RCT or non-RCT

Q4. Is the risk of lymph node metastasis higher in the submucosal invasive colorectal cancer with tumor budding than in the submucosal invasive colorectal cancer without tumor budding?

Patient: Patients who were diagnosed with submucosal colorectal cancer
Patient: Patients who were diagnosed with submucosal colorectal cancer with tumor budding
Comparator: Patients who were diagnosed with submucosal colorectal cancer without tumor budding
Outcome: Incidence of lymph node metastasis
Study design: RCT or non-RCT

Q5. Is the risk of lymph node metastasis higher in the poorly differentiated early colorectal cancer than in the well or moderately differentiated early colorectal cancer?

Patient: Patients who were diagnosed with early colorectal cancer
Intervention: Patients who were diagnosed with poorly differentiated early colorectal cancer
Comparator: Patients who were diagnosed with well or moderately differentiated early colorectal cancer
Outcome: Incidence of lymph node metastasis
Study design: RCT or non-RCT

Statement C2: Endoscopic resection of submucosal colorectal cancer with a high risk of lymph node metastasis has a higher recurrence rate than surgical resection. Therefore, we recommend additional surgery if histological signs after endoscopic resection suggest a high risk of lymph node metastasis. (Grade of recommendation: strong, Level of evidence: high)

Q1. Are the recurrence and survival rates different between the endoscopic resection and the surgical resection for the submucosal invasive colorectal cancer with low risk of lymph node metastasis?

Patient: Patients who were diagnosed with submucosal colorectal cancer with low risk of lymph node metastasis
Intervention: Endoscopic resection
Comparator: Surgery
Outcome: Recurrence and/or survival rates
Study design: RCT or non-RCT

Q2. Are the recurrence and survival rates different between the endoscopic resection and the surgical resection for the submucosal invasive colorectal cancer with high risk of lymph node metastasis?

Patient: Patients who were diagnosed with submucosal colorectal cancer with high risk of lymph node metastasis
Intervention: Endoscopic resection
Comparator: Surgery
Outcome: Recurrence and/or survival rates
Study design: RCT or non-RCT

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Statement C3: We recommend endoscopic assessment of pit patterns and vascular patterns to estimate the depth of submucosal invasion before endoscopic resection of early colorectal cancer. (Grade of recommendation: strong, Level of evidence: high)

Q1. For the diagnosis of suspected/established early colorectal cancer, is narrow band imaging useful to differentiate mucosal/superficial submucosal cancer from deep submucosal cancer compared with white light endoscopy?

Patient: Patients who have suspected or established early colorectal cancer
Intervention: Narrow band imaging
Comparator: White light endoscopy
Outcome: Differentiation of mucosal/superficial submucosal cancer from deep submucosal cancer (diagnostic accuracy)
Study design: RCT or non-RCT

Q2. For the diagnosis of suspected/established early colorectal cancer, is chromoendoscopy useful to differentiate mucosal/superficial submucosal cancer from deep submucosal cancer compared with white light endoscopy?

Patient: Patients who have suspected or established early colorectal cancer
Intervention: Chromoendoscopy
Comparator: White light endoscopy
Outcome: Differentiation of mucosal/superficial submucosal cancer from deep submucosal cancer (diagnostic accuracy)
Study design: RCT or non-RCT

Q3. For the diagnosis of suspected/established early colorectal cancer, is magnifying endoscopy useful to differentiate mucosal/superficial submucosal cancer from deep submucosal cancer compared with conventional endoscopy?

Patient: Patients who have suspected or established early colorectal cancer
Intervention: Magnifying endoscopy
Comparator: Conventional (non-magnifying) endoscopy
Outcome: Differentiation of mucosal/superficial submucosal cancer from deep submucosal cancer (diagnostic accuracy)
Study design: RCT or non-RCT

Statement C4. En bloc and histologically complete resection should be achieved for endoscopic treatment of a suspected or established early colorectal cancer. We recommend endoscopic submucosal dissection for the treatment of endoscopically resectable early colorectal cancer which cannot be resected en bloc using endoscopic mucosal resection technique. (Grade of recommendation: strong, Level of evidence: moderate)

Q1. Does endoscopic submucosal dissection provide higher en bloc resection rate for suspected or established early colorectal cancer than endoscopic mucosal resection or other endoscopic resection techniques?

Patient: Patients who have suspected or established early colorectal cancer
Intervention: Endoscopic submucosal dissection
Comparator: Endoscopic mucosal resection, endoscopic resection techniques other than endoscopic submucosal dissection
Outcome: En bloc resection rate
Study design: RCT or non-RCT