

Supplementary Materials

Appendix A

Analysis of relevant literature 1: The definition of SMIS was proposed by Professor Enqiang Linghu in 2016 and subsequently published in both Chinese and English journals, including *Chin Med J (Engl)*, *World J Gastroenterol*, and the *Chinese Journal of Gastrointestinal Endoscopy*.^[1-6] Numerous clinical studies have also confirmed that, compared to traditional open or extensive resection surgeries, SMIS significantly reduces surgical trauma, preserves organ function, lowers the risk of complications, and comprehensively enhances the postoperative physiological functions, psychological health, and social adaptability of patients, in addition to ensuring effective tumor treatment.^[7-9] A single-center propensity score-matched study showed that SMIS had the same curative effect as traditional esophagectomy for the treatment of superficial esophageal squamous cell carcinoma. However, the SMIS group had significantly shorter operative times and hospital stays, less intraoperative blood loss, and a lower incidence of postoperative complications (such as pulmonary infection and anastomotic leakage) compared to the esophagectomy group.^[7] Six months post-surgery, the SMIS group had significantly better swallowing function, nutritional status, and overall quality of life (as measured by the EORTC QLQ-C30 scale) than the traditional esophagectomy group, particularly in terms of preserving the esophageal physiological structure and reducing reflux symptoms.^[7] Another single-center propensity score-matched study evaluated the impact of SMIS and proximal gastrectomy on the health-related quality of life in patients with early esophagogastric junction adenocarcinoma, which found that the SMIS group retained better gastric volume, had a 50% lower incidence of reflux esophagitis, and experienced significantly less postoperative weight loss than the traditional surgery group. Twelve months post-surgery, the SMIS group scored significantly better than the proximal gastrectomy group in physical function, social role functioning, and emotional health (as measured by the SF-36 scale), and had fewer dietary restrictions. The study concluded that SMIS effectively maintained digestive function by removing lesions while preserving organs, which significantly improved postoperative quality of life and psychological

adaptability.^[10] A cross-sectional study comparing the effects of organ-preserving surgery and organ resection on bowel function, psychological health, and quality of life in patients with ECRC showed that the SMIS group had significantly better postoperative bowel frequency and fecal incontinence control (Wexner score), with a 60% reduction in the incidence of bowel dysfunction. The SMIS group also had significantly lower levels of anxiety and depression (as measured using the HADS scale), higher satisfaction with postoperative appearance and autonomy, and a better overall quality of life, with higher scores in physical health, social relationships, and psychological health dimensions (as measured by the WHOQOL-BREF scale) compared to the resection group(8). SMIS, while providing radical treatment of early colorectal tumors, was also concluded to maximally preserve organ function and significantly improve postoperative physical and psychological health, rendering it the preferred option for enhancing quality of life.

Analysis of relevant literature 2: A review published in the *Chinese Journal of Digestive Endoscopy* in 2021 first clarified that digestive endoscopic SMIS was implemented through four types of channels using dozens of methods, and detailed the surgical techniques and methods using different channels (including hemostasis, traction, and closure).^[11] Two case reports demonstrated that the through-the-scope twin clip closure method based on SMIS effectively closed large digestive tract defects.^[12, 13] One case report described the SMIS-based method of “simultaneous incision and conventional tissue clip closure” for the immediate closure of perforated defects during surgery, which effectively prevented gas and fluids from entering the abdominal cavity, and thus avoided abdominal infections.^[14] A single-center retrospective study showed that the use of rubber band traction methods accelerated the efficiency of SMIS in non-FTR of colorectal lesions and assisted in closing large defects.^[15] Another single-center retrospective study indicated that the tissue clip-dental floss adjustable angle traction method enhanced the efficiency of SMIS for non-FTR of gastric lesions and effectively prevented perforation complications.^[16]

Analysis of relevant literature 3: In 2024, the principles for the implementation of digestive endoscopy-based SMIS were explicitly outlined in the *Chinese Journal of*

Medical Sciences, providing a scientific framework for the safe and reliable conduct of SMIS.^[17] In 2023, the “Expert Consensus on Wound Preparation and Antibiotic Application for Digestive Endoscopy Super Minimally Invasive Surgery” consensus statement^[18] was published, followed by an expert interpretation of its contents in the same year. This consensus offers guidance for perioperative preparation of digestive endoscopy SMIS.^[19]

Analysis of relevant literature 4: The term “SMIS” was clearly defined, along with its usage and nomenclature conventions, in the book *Digestive Endoscopy Terminology*^[5] published by the China National Committee for Terminology in Science and Technology in 2021. In 2023, the interpretation of the terminology of the book was examined.^[20] The monograph *Digestive Endoscopy: Super Minimally Invasive Surgery*, published in 2025, uniformly applied the resulting nomenclature convention.^[21] Additionally, several clinical studies have adhered to this nomenclature convention.^[8,15,16,22-26]

Evidence summary 5: A systematic search and screening of 49 articles led to the inclusion of 10 relevant studies that were comprehensively analyzed. A multicenter prospective study in France ($n = 195$) reported a complete resection rate of 100% for early adenocarcinoma and Barrett’s esophagus with HGIN treated with ESD, with an R0 resection rate of 78.5% and a curative resection rate of 67.2%. The intraoperative perforation rate was only 0.5%, but the postoperative stricture rate was 15.9%, indicating that extensive resection should be combined with preventive measures.^[27] A prospective study in Denmark ($n = 132$) comparing ESD with EMR found that the complete resection rate (98.8% vs. 64.1%) and R0 resection rate (83.9% vs. 23.8%) were significantly higher with ESD ($P < 0.001$). Although the complication rate was higher with ESD (28.7% vs. 3.1%), the local recurrence rate was lower (14.5% vs. 23.8%).^[28] A Chinese multicenter RCT ($n = 40$) of lesions with 50% or more circumferential involvement confirmed that ESTD was associated with a faster dissection speed ($P = 0.047$), less muscular layer damage ($P < 0.05$), and a higher mucosal healing rate one month postoperatively compared to traditional ESD.^[29] A single-center prospective study in China ($n = 40$) comparing ESTD and ESD for early

squamous cell cancer involving 50% or more of the esophageal circumference showed that the dissection speed in the ESTD group was significantly faster than in the ESD group ($P = 0.047$), but there were no significant differences between the two groups in terms of operation time, dissection area, complete resection rate, R0 resection rate, or complication rate.^[30] Several meta-analyses confirmed that ESD had significantly better complete resection rates, R0 resection rates, and recurrence risks than EMR, and the dissection speed of ESTD is superior to that of ESD.^[9,29-33] The ASGE guidelines (2023)^[34] recommend prioritizing ESD for lesions > 15 mm (evidence level: moderate) and emphasize its role in accurate staging and reducing recurrence risk, and the AGA guidelines (2020)^[35] clearly identify endoscopic surgery as the preferred treatment for high-grade dysplasia or mucosal cancer in Barrett's esophagus and suggest it as an alternative to esophagectomy for low-risk T1b lesions. Additionally, a Brazilian meta-analysis incorporating 15 observational studies (as of July 28, 2023, with 9352 patients, including 2537 in the ESD group and 6,815 in the EMR group) found that the ESD group had significantly higher complete resection rates (OR = 25.96) and R0 resection rates (OR = 5.10), with a lower recurrence rate (3.08% vs. 11.69%, OR = 0.22).^[36]

Evidence summary 6: Through a systematic search and selection of 49 articles, 7 relevant studies were ultimately used in a comprehensive analysis. A Chinese single-center prospective study ($n = 81$) showed that oral corticosteroids alone or combined with local corticosteroid injection effectively prevented post-ESD esophageal stricture and reduced the number of post-operative dilations, with the combination therapy more effective.^[37] A Chinese single-center prospective study ($n = 70$) demonstrated that a combination of polyethylene glycol and stent placement more effectively prevented post-ESD esophageal stricture in patients with EEC than stent placement alone.^[38] Another Chinese single-center prospective study ($n = 63$) showed that an aluminum phosphate gel was significantly more effective than triamcinolone acetonide injection with oral prednisone in preventing post-ESD esophageal stricture when the circumferential mucosal defect was greater than 75%, with a stricture rate of 9.4% versus 35.5% (best cut-off values: 97.9% vs. 90.6%).^[39] Furthermore, a Chinese prospective study ($n = 28$) demonstrated that esophageal stent placement was a safe and

effective method for preventing post-ESD esophageal stricture, particularly for patients with mucosal defects exceeding 75% of the esophageal circumference.^[40] Two meta-analyses from China, both showing positive results, focused on strategies to prevent post-ESD esophageal stricture in patients with EEC.^[41,42]

Evidence summary 7: Through a systematic search and screening of 191 articles, ultimately 56 relevant studies were selected for comprehensive analysis. Sixteen single-center prospective studies from China and South Korea demonstrated that a comprehensive evaluation of the postoperative observation indicators reported in the literature for EGC after surgery revealed no significant difference between endoscopic surgery and “organ resection, reconstructive” surgery in terms of overall patient survival. However, endoscopic surgery was superior regarding rates of curative resection, postoperative complications, and postoperative quality of life.^[43-58] Fifteen meta-analyses confirmed that there was no significant difference between endoscopic surgery and “organ resection, reconstructive” surgery in terms of overall patient survival. However, endoscopic surgery has demonstrated a significant advantage in the incidence of postoperative complications and postoperative quality of life, although it is not superior to “organ resection, reconstructive” surgery regarding the rate of curative resection.^[32,59-72] Multiple retrospective studies from research centers in China, South Korea, Japan, Lithuania, and Rome confirmed there was no significant difference between endoscopic surgery and “organ resection, reconstructive” surgery in terms of overall patient survival. Endoscopic surgery was superior regarding the incidence of postoperative complications and postoperative quality of life, and was not inferior to “organ resection, reconstructive” surgery in terms of the rate of curative resection.^[73-85] The American Society for Gastrointestinal Endoscopy (ASGE) clearly states in the Summary and Recommendations section of its guideline “Endoscopic Submucosal Dissection for the Management of Early Esophageal and Gastric Cancers”^[34] that surgical resection is not required for EGC lesions that are well or moderately differentiated, are of an intestinal type, and have a maximum diameter of 3 cm. The guidelines^[86] from the British Society of Gastroenterology regarding the diagnosis and management of patients at risk for GC suggest that all gastric mucosal dysplasia and EGC should undergo en bloc resection. EMR can achieve en bloc resection of lesions

≤ 10 mm, but only ESD can ensure en bloc resection of lesions > 10 mm. (Evidence level: High quality; Recommendation level: Strong; Agreement level: 100%). According to the “Clinical Practice Guidelines for Endoscopic Resection of Early Gastrointestinal Cancer”,^[87] (1) for well or moderately differentiated tubular adenocarcinomas or papillary adenocarcinomas with a tumor maximum diameter ≤ 2 cm and diagnosed as mucosal cancer without ulcer formation during endoscopy, endoscopic resection is strongly recommended (recommendation level: strong; evidence level: moderate); (2) for lesions with similar histological characteristics, endoscopic resection is recommended when any of the following conditions are met: (i) mucosal cancer with a maximum diameter > 2 cm but no ulcer, or (ii) mucosal cancer with a maximum diameter ≤ 3 cm accompanied by an ulcer (recommendation level: weak; evidence level: moderate); and (3) for poorly differentiated tubular adenocarcinomas, low-adhesion cancer, or signet-ring cell cancer, if the maximum diameter of the tumor is ≤ 2 cm, endoscopic resection may be considered if the endoscopic evaluation is mucosal cancer without accompanying ulcers (recommendation level: weak; evidence level: low). According to the European Society of Gastrointestinal Endoscopy (ESGE) guidelines,^[88] (1) for gastric superficial tumor-like lesions with an extremely low risk of LNM, endoscopic resection is strongly recommended (recommendation level: strong; evidence level: high); (2) for lesions with a diameter < 15 mm and a low risk of histological progression, EMR may be considered as a treatment option; and (3) for most gastric superficial tumor-like lesions, ESGE preferentially recommends ESD as the standard treatment option (recommendation level: strong; evidence level: moderate). Furthermore, the consensus on the detection and treatment of EGC in Mexico^[89] suggests that endoscopic treatment should be performed for patients whose lesions are of a size that allows complete resection of a single specimen and whose risk of LNM is extremely low (evidence quality: C1 level; recommendation level: strong, in favor; consensus: fully agree 82%, partially agree 18%). The 2021 “Japanese Gastric Cancer Treatment Guidelines (6th edition)”^[90] propose considering endoscopic resection for tumors with a very low possibility of LNM and those suitable for complete resection.

Evidence summary 8: Through a systematic search and screening of 144 articles,

19 relevant studies were included for comprehensive analysis. Several meta-analyses indicate that, compared to laparoscopic D2 radical surgery for EGC, ESD treatment showed similar survival rates and recurrence-free rates. Moreover, ESD-treated patients had shorter hospital stays, faster recoveries, and lower adverse event rates, and thus avoided overtreatment.^[59-61,70-72,91-93] A multicenter retrospective study in Germany suggested ESD as the standard treatment for EGC(94). A single-center retrospective study in China ($n = 324$) indicated that over one-third of EGC patients treated surgically may achieve a cure through ESD.^[95] Two single-center retrospective studies in China suggested that patients with undifferentiated EGC can also achieve curative resection through ESD.^[96,97] A single-center retrospective study in China ($n = 27$) highlighted the limitations of EMR and ESD in LN clearance and the significant surgical complications associated with total gastrectomy. The study proposed that a distal gastrectomy with regional LN dissection for early gastric body cancer may avoid overtreatment and excessive surgery.^[98]

Evidence Summary 9: Through systematic retrieval and screening of 146 studies, a total of 2 relevant studies were included for comprehensive analysis. A review introduced the concept, methods, and application prospects of the SMIS-Cure evaluation system.^[99] A single-center prospective single-arm study ($n = 8$) in China showed that all eight patients with EGC successfully underwent safe sft-SMIR, achieving curative resection. The SMIS-Cure degree evaluation system was applied, and the results showed that there were seven cases of SMIS-Cure A (cured) and one case of SMIS-Cure B2 (clinically cured).^[100] The establishment of the SMIS-Cure evaluation system provides a systematic framework for evaluating the cure degree of SMIS surgery for EGC, which has important clinical value and offers a clear basis for medical personnel to make treatment decisions. It should be noted that the current validation of the SMIS-Cure system for GC is still at a preliminary stage. The available evidence comes from only two studies—one review article and a small prospective study with 8 cases—which corresponds to a low level of evidence. Therefore, while the concept of the SMIS-Cure system is novel and promising, its clinical utility has yet to be confirmed. Future large-scale, multicenter studies are warranted to further evaluate

and validate this system, and it should presently be considered an important direction for ongoing research.

Evidence Summary 10: Through a systematic search and screening of 144 studies, three relevant studies were included for comprehensive analysis. According to the guidelines of the American Society for Gastrointestinal Endoscopy (2023 edition), different endoscopic follow-up strategies should be adopted for digestive tract lesions at different stages. For patients with high-grade and low-grade intraepithelial neoplasia of the stomach, endoscopic monitoring is recommended every 6 months in the first 2 years after diagnosis, and then adjusted to an annual endoscopic follow-up. For patients with T1a GC, endoscopic follow-up is recommended 3 to 6 months in the first year after surgery. The endoscopic follow-up interval can be extended to 6 to 12 months in the second and third years after surgery, and then finally switched to an annual routine endoscopic follow-up. In cases of T1b with negative lateral and basal resection margins (R0 resection), endoscopic follow-up is recommended 3 to 6 months in the first year after surgery, and then annually. An imaging evaluation should also be included, with CT examinations recommended every 6 to 12 months within 3 to 5 years after surgery to rule out potential metastasis risks. According to “The Mexican consensus on the detection and treatment of EGC”,^[89] after endoscopic radical resection for EGC, endoscopy recheck is recommended 6 to 12 months after surgery to monitor metachronous GC (Evidence quality C1; Recommendation strength: Strong; 82% of people strongly agree, and 18% partially agree). According to the recommendations of the “Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition)”^[90] different management strategies should be adopted after endoscopic resection of GC at different stages. For patients in the eCure A stage, endoscopic follow-up is recommended yearly after surgery. For patients in the eCure B stage, monitoring must be strengthened, with 1 or 2 endoscopic examinations combined with abdominal ultrasound or CT evaluation recommended each year. Regardless of stage, the guidelines emphasize routine *Helicobacter pylori* testing after surgery, and if the result is positive, eradication treatment should be carried out in a timely manner. Due to the long-term risk of metachronous GC, a long-term follow-up plan should be established for all patients. In eCure C1 stage cases, if the lesion is a differentiated GC ≤ 3 cm and has any of the

characteristics of UL1, pT1a (M), or pT1b1 (SM1), the range of residual mucosal lesions must be re-evaluated through endoscopy. When the total length of the primary focus and the residual focus exceeds 3 cm, the guidelines clearly list gastrectomy combined with LN dissection as the standard treatment plan. For patients in the eCure C2 stage, gastrectomy combined with LN dissection is recommended as the standard treatment method.

Evidence summary 11: Through systematic retrieval and screening of 168 studies, a total of 10 relevant studies were selected for comprehensive analysis. A single-center prospective study in Japan ($n = 300$) showed that a decrease in hemoglobin of ≥ 2 g/dl was observed in 5% of ESD cases (LAC: 30.0%). Complications occurred in 7% of ESD cases (LAC: 15%). The incidences of delayed bleeding and perforation were 5 and 1.7% of ESD cases, respectively. Although only one patient required laparotomy for peritonitis caused by delayed perforation, other patients could be treated endoscopically. Due to the redefinition of the risk of LNM, 16 ESD cases required additional LAC. The median length of the hospital stay for ESD was 5 days (LAC: 10 days).^[101] A multicenter prospective study in the Netherlands ($n = 1315$) indicated that additional surgery should only be considered for patients with high histological risk or positive resection margins after endoscopic resection.^[102] A single-center prospective study in China ($n = 120$) showed that the operation time, recovery time of gastrointestinal function, length of hospital stay, and treatment costs of patients in the ESD group were significantly better than those in the conventional surgical resection group ($P < 0.05$), and the negative margin rate of tumors in the ESD group was significantly lower than in the conventional surgical resection group ($P < 0.05$).^[103] One meta-analysis reported positive results suggesting that compared with surgery, the operation time and length of hospital stay of the ESD group were better than those of the surgical group. However, the en bloc resection rate and radical resection rate in the ESD group were lower, but there was no significant difference in postoperative complications or the recurrence rate between the two groups (104). A multicenter retrospective study in Japan ($n = 701$) showed that ER for T1 CRC did not deteriorate the clinical outcomes of patients who required additional surgical resection.^[105] There were a total of four single-center retrospective studies, all of which suggested that minimally invasive endoscopic

treatment was as effective as surgery but less invasive, and that it could become the first-line treatment for ECRC.^[106-109] A prospective multicenter cohort study from Japan and Greece included 23 patients treated with EID who had either deep submucosal invasive RC, scarred and severely fibrotic rectal lesions, or benign tumors. The results showed that there were no serious complications in any patients; pain was reported in four cases, transient urinary incontinence occurred in one case, postoperative stricture occurred in one case that was supplemented with dilation treatment, and incomplete resection of a T2 tumor was found in one case. The EID surgical resection plane entered the intermuscular space between the longitudinal (external) and circular (internal) muscle layers. This technique showed great potential for endoscopic radical resection of invasive rectal submucosal cancer.^[110]

Evidence Summary 12: Through a systematic search and screening of 216 articles, a total of 11 relevant studies were selected for comprehensive analysis. A multicenter prospective study in the Netherlands ($n = 67$) showed that the final complete resection rate and curative resection rate of EID for colorectal tumors were 96 and 81%, respectively. The average operation time (standard deviation) was 110 ± 51 min, and the average tumor size was 25 mm. Minor adverse events occurred in 8 patients, with moderate perianal pain in three patients (4%) and inflammatory reactions (fever, pain, elevated C-reactive protein, but no fluid accumulation in the perirectal air) in 3 patients (4%). All patients were conservatively treated with intravenous antibiotics and/or analgesics.^[111] In a single-center prospective study in Japan ($n = 23$), 22 of 23 patients with colorectal tumors underwent en bloc endoscopic complete resection (96%, 95% CI: 90%–99%), while the complete dissection rate of benign scar lesions was 100% (12/12), confirming that EID ensured margin-free resection, or at least provided accurate diagnostic pathological support for prospective oncological surgery of T2 tumors.^[110] Multiple meta-analyses have shown that compared with EMR, ESD is associated with more postoperative complications, including perforation and bleeding, but has a higher R0 resection rate and better prognosis. Therefore, ESD is more often recommended for patients with ECRC. Compared with TEM, ESD had fewer postoperative complications, with no significant difference in the R0 resection rate.^[112-116] A single-center retrospective study in China used an endoscopic and laparoscopic

combined surgery for treatment. Patients with T2 CRC underwent FTR, and peripheral LN dissection was performed. Different endoscopic treatment methods were selected according to risk stratification of ECRC to formulate a precise treatment strategy for patients.^[117] A multicenter prospective study in Denmark ($n = 25$) treated patients with CRC (cT1-2cN0cM0) with combined endoscopic-laparoscopic surgery (CELS) and concluded that in select patients, CELS resection was feasible and avoided colectomy.^[118] According to the ESGE guidelines (2024),^[119] in the treatment of suspected superficial invasive cancer, if standard polypectomy or EMR cannot achieve complete resection, the following techniques are recommended as the preferred options: EMR, ESD, EID, EFTR, or surgical resection with complete resection (Evidence level: moderate). The NCCN *Clinical Practice Guidelines in Oncology*^[120] indicated that compared with EMR, the main advantages of ESD are a higher en bloc resection rate and a lower recurrence rate; the disadvantages are a longer operation time, a higher complication rate, and a steep learning curve. According to the morphology of the lesion, colorectal ESD can be considered for lesions with a high suspicion of limited superficial mucosal invasion. For T2 CRC, due to the higher risk of LNM, FTR and LN dissection are recommended. A meta-analysis from China included five RCTs and eight cohort studies. The results showed that compared with radical surgery, TEM was associated with a higher risk of local recurrence, but had advantages regarding disease-free survival, reduction of perioperative mortality, temporary stoma, permanent stoma, and postoperative complications. TEM also effectively shortened the operation time, postoperative bleeding, and hospital stay. There were no statistically significant differences between the two surgical approaches in terms of the incidence of distant metastasis, overall recurrence, or disease-specific survival rates.^[121] A randomized controlled trial in China compared the data of 60 patients with T1-2N0 RC who underwent TEMS and laparoscopic anterior resection (LAR). The results showed that the operation time and postoperative defecation recovery time in the TEMS group were significantly shorter than those in the LAR group, with the postoperative defecation recovery time earlier (1 day vs. 3 days). The complications in both groups were generally mild and self-limiting; however, two patients at T2 stage in the TEMS group (2/28, 7.1%) had local recurrences (8 months and 16 months after surgery), while there

were no recurrences in the LAR group (0/30), suggesting that although TEMS accelerated postoperative recovery and reduced surgical risks, its local control ability of T2 tumors needs to be carefully evaluated.^[122]

Evidence Summary 13: Through a systematic search and screening of 225 studies, 13 relevant studies were included for a comprehensive analysis. A multicenter prospective study in Japan ($n = 1090$) showed that the final complete resection rate and curative resection rate of patients with colorectal tumors treated with ESD were 88% and 89%, respectively.^[123] A meta-analysis in China compared the efficacy of ESD and EMR in the treatment of DTTs, with positive results. The study suggested that compared with EMR, ESD showed a better complete resection rate, curative resection rate, and lower local recurrence rate, but with a longer operation time and a higher incidence of bleeding and perforation complications.^[124] A multicenter retrospective study in Germany ($n = 1234$) showed that the R0 resection rate of patients who received EFTR treatment due to various indications was 71.8%(125). A multicenter retrospective study in Belgium and Portugal ($n = 252$) showed that the R0 resection rate of rectal ESD cases was 75%, and the curative resection rate was 70%(126). There were a total of nine single-center retrospective studies, all with positive results, with significant differences in diseases and stages in these studies.^[127-135] The 2022 version of the NCCN “Guidelines for Colorectal Cancer”^[136] proposed that for malignant polyps with complete resection and good histological features, resection is usually considered curative, and no additional surgery is required. If adverse histological features are found, further examinations (such as imaging) may be needed, and surgeries such as colectomy may be required. The 2023 CSCO “Colorectal Cancer Guidelines”^[137] propose a structured and layered optimization of endoscopic treatment for T1N0 stage colon cancer. Complete resection is recommended for flat lesions (diameter 5–20 mm), extensive lesions suspected to be villous adenomas or extensive serrated adenomas (> 10 mm), or suspected HGIN (≤ 20 mm) (EMR is recommended for grade I, ESD is recommended for grade II). For some T1 stage colon cancer (submucosal infiltration < 1 mm), laterally developing tumors (LST ≥ 20 mm), or fibrotic villous adenomas (≥ 25 mm), ESD is recommended if grade I, and surgical treatment is recommended if grade II. To determine curative resection, the following histological criteria must be

met: submucosal infiltration depth < 1 mm, no lymphatic vessel invasion, good tumor differentiation, zero tumor budding, and negative margin (≥ 1 mm from the margin). In terms of postoperative management, follow-up endoscopy is recommended 3–6 months after surgery for patients with unclear surgical margins, and 1 year after surgery for patients with negative surgical margins. The 2020 version of the ESMO “Guidelines for Local Colon Cancer”^[138] proposed that for hyperplastic or adenomatous polyps and non-invasive adenocarcinoma (pTis, intraepithelial or intramucosal), endoscopic resection is sufficient. For invasive cancer (pT1), the treatment method depends on the polyp morphology and the presence of histological features associated with a poor prognosis. For pedunculated polyps with pT1 cancer limited to the head, neck, and stalk (Haggitt 1–3) without unfavorable factors, even if there is submucosal invasion, endoscopic resection and appropriate follow-up are sufficient. However, for patients with an average surgical risk, if sessile or flat polyps (Paris classification) are associated with pT1 cancer and there are any unfavorable factors, surgical resection must be performed. A positive resection margin (< 1 mm) only constitutes a risk of local recurrence, which can be managed with repeated resection or local monitoring. If surgery is not possible due to severe comorbidities, colonoscopic monitoring is recommended within 6 months after polypectomy, with close oncological follow-up, including CT scans to detect LN recurrence. The 2019 version of the JSCCR “Guidelines for Colorectal Cancer”^[139] proposed that for piecemeal resection of sheet-like pTis cancer with positive horizontal margins, local recurrence should be checked by colonoscopy around 6 months. In the follow-up observation of pT1 cancer, local recurrence, LN recurrence, and distant metastasis recurrence should be evaluated. The follow-up should include endoscopic examination, imaging diagnosis, and tumor marker evaluation. According to “Expert Consensus on Management Strategies for Precancerous Lesions and Conditions of Colorectal Cancer in China”^[140] the preferred method for endoscopic resection of early CRC and HGIN is ESD. In cases with positive vertical margins in postoperative pathology, additional treatment should be considered after confirming residual lesions. If the lesion has been completely removed and meets the following five conditions simultaneously, it can be considered as achieving curative resection: negative vertical margin; pathological type of papillary adenocarcinoma or

tubular adenocarcinoma; submucosal infiltration depth < 1000 μm; no vascular invasion; and tumor budding is grade 1 (low grade). If any of the above five conditions are not met, a comprehensive assessment of the risk of LNM and the specific situation of the patient (including age, underlying diseases, physical condition, personal wishes, and postoperative quality of life) is required to determine whether additional surgery is needed. In addition, in cases with positive vertical margins due to technical limitations, after a detailed evaluation, endoscopic resection may be considered again. An expert consensus on endoscopic diagnosis and treatment of CRC and precancerous lesions in China (2023, Guangzhou)^[141] proposed that if the postoperative pathology report indicates that the epithelial tumor has not penetrated the muscularis mucosae and invaded the submucosa, and the resection margin is negative, it is regarded as a complete and curative resection, and no additional treatment is required.

Evidence summary 14: Through a systematic search and screening of 145 articles, 12 relevant studies were selected for comprehensive analysis. A prospective study involving 362 patients with locally advanced non-metastatic RC ($\geq T3$ or Tany N+ any without distant metastasis) showed that there were no significant differences in the overall survival rate (85.6% vs. 93.3%, $P = 0.414$) or disease-free survival rate (78.3% vs. 80%, $P = 0.846$) between radical surgery and LE.^[142] A multicenter prospective study in France showed that among 74 patients in the LE group, 26 patients subsequently underwent TME surgery, and it could not be confirmed that LE was superior to TME.^[143] A multicenter prospective study in the Netherlands included 55 RC patients with an expecting treatment response after long-course concurrent chemoradiotherapy. Eventually, 47 patients received TEM, with a 5-year overall survival rate of 82.8%.^[144] A prospective cohort study in the Netherlands included 67 patients with suspected deep submucosal invasive RC who underwent EID. The overall technical success rate of the treatment was 96%, the R0 resection rate was 81%, and the radical resection rate was 45%.^[111] A meta-analysis in China included four retrospective cohort studies and seven prospective non-randomized controlled trials (a total of 1131 patients). By comparing the effectiveness and safety of the W&W strategy, radical surgery, and LE in RC patients with a cCR after neoadjuvant chemoradiotherapy, it was found that the local recurrence rate in the W&W group was higher than in the

radical surgery group, and there were no significant differences in distant metastasis and mortality rates among the three groups of patients.^[145] Two Chinese case series studies included patients who achieved cCR or near-CR after neoadjuvant chemoradiotherapy and LE, but experienced local recurrence and distant metastasis upon follow-up. Both studies suggested that for RC patients evaluated as having cCR after receiving neoadjuvant chemoradiotherapy and undergoing LE due to a strong desire to preserve the anus, LE has certain diagnostic and therapeutic value, but the indications must be strictly selected.^[146,147] A retrospective study compared the prognosis of RC patients who achieved cCR after chemoradiotherapy and received radical surgery (37 patients) and those who received only LE (14 patients). The disease-free survival rate, pelvic recurrence-free survival rate, and overall survival rate of the two groups of patients were similar.^[148] A Chinese retrospective cohort study compared the efficacy of TEM and transanal total mesorectal excision (taTME) and found that the 5-year progression-free survival rates of the two groups were similar.^[149] “Expert Consensus on the Early Diagnosis and Treatment of Colorectal Cancer in China” (2023 edition)^[150] recommends intersphincteric resection (ISR) as an option for ultra-low anal-preserving surgery for patients with cT1 stage ultra-low and low RC not suitable for LE, and for some RC patients whose cancer was downstaged after preoperative chemoradiotherapy. For cT1N0M0 RC patients with high-risk factors for metastasis and a strong desire to preserve the anus, concurrent chemoradiotherapy combined with LE (including TEM and TAMIS) can be adopted (Recommendation level: Strong; GRADE classification: moderate). The ESMO “Guidelines for Rectal Cancer”^[151] recommend that for low cT3a and cT3b, medium and high cT3a and cT3b, and cN1–2 RC with negative mesorectal fascia and negative extramural vascular invasion, TME surgery can be directly performed; the treatment strategy for the remaining LARC is the “sandwich treatment” of preoperative concurrent chemoradiotherapy, TME surgery, and postoperative adjuvant chemotherapy. The “Chinese Expert Consensus on the Watch-and-Wait Strategy after Neoadjuvant Therapy for Rectal Cancer” (2024 edition)^[152] recommends that for patients with a stage of ycT1N0M0 after neoadjuvant therapy, patients in which there is difficulty preserving the anus, and patients with a strong desire to preserve the anus, LE can be selected. (Evidence level: III,

Recommendation level: B level, Expert group approval rate: 96.77%). A meta-analysis in the UK included 17 studies, of which 10 were retrospective cohort studies and 4 were prospective studies. The results showed that the 2-year local recurrence rate using the W&W strategy was 15.7%, the 3-year local recurrence rate was approximately 22%, and the vast majority of patients chose supplementary surgery after local recurrence.^[153,154] A retrospective observational study in the United States ($n = 249$) analyzed and compared the W&W strategy of patients who achieved cCR after completing neoadjuvant therapy and in rectal adenocarcinoma patients who received TME and achieved a pCR. The results showed that the 5-year disease-free survival rate, overall survival rate, and disease-specific survival rate in the W&W group were all inferior to those of TME. Furthermore, in the W&W group, the survival rate of patients with local recurrence was poorer, and the incidence of distant progression was higher.^[155]

Evidence summary 15: A meta-analysis that included 29 studies with a total of 1,751 patients indicated that for the treatment of ampullary neoplastic lesions by SMIS-EP, the en bloc resection rate was 82.4% (95% CI: 74.7%–88.1%), and the radical resection rate was 87.1% (95% CI: 83.0%–90.3%). The overall incidence of adverse events was 24.9% (95% CI: 21.2%–29.0%), among which postoperative pancreatitis was the most common, accounting for approximately 11.9% (95% CI: 10.4%–13.6%).^[156] A retrospective study published in *Gut* in 2025,^[157] which involved 1673 patients from 58 centers in Europe and the United States, showed that by treating ampullary adenoma by endoscopic resection, the R0 resection rate was 80.2% (386/481), the incidence of severe adverse events was 1.9% (11/569), there were no deaths, and the average follow-up period was 20 months (ranging from 9 to 46 months), with a recurrence rate of approximately 13.5% (65/481). After propensity score matching, the R0 resection rates of endoscopic resection and surgical papillectomy were 72.6% and 90.3% respectively ($P = 0.02$), with no significant difference in the recurrence rate (8% vs. 3.2%, $P = 0.07$) or survival rate between the two groups. However, there was one death in the surgical group, and the operation time and hospital stay in the endoscopic group were significantly shorter than those of the surgical group (36 min vs. 225 min, 3 days vs. 14 days, $P < 0.001$). Postoperative recurrence is a matter

of widespread concern. In 2023, Garg *et al.*^[158] published a meta-analysis (39 studies with 1753 patients) comparing endoscopic resection with surgical resection to evaluate postoperative recurrence. The 1-, 2-, 3-, and 5-year recurrence rates of endoscopic resection (13.0%, 12.5%, 13.3%, and 15.7%, respectively) and surgical resection (14.1%, 14.3%, 12.9%, and 17.6%, respectively) showed no significant difference ($P > 0.05$). Internationally, guidelines developed by multiple societies such as those in Europe, France, and Japan (*e.g.*, ESGE, JGES) all recommend endoscopic papillectomy as the treatment of choice for duodenal papillary adenoma.^[159-161]

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