Cancer Biol Med 2026. doi: 10.20892/j.issn.2095-3941.2025.0784

CONSENSUS

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Chinese expert consensus on additional surgery following endoscopic resection for early colorectal cancer (2025 edition)

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ABSTRACT Early colorectal cancer is often treated through endoscopic procedures to remove tumors. However, when initial removal is incomplete or shows high-risk features, further major surgery is required to ensure no cancer remains. This consensus provides a standard for surgeons to decide when and how to perform this additional surgery. A multidisciplinary group of Chinese medical experts reviewed global research and clinical evidence published between 2010 and 2024. The medical experts formulated key clinical recommendations, which were then discussed and finalized through expert voting to ensure high agreement. The consensus identifies specific high-risk factors necessitating additional surgery. The consensus recommends that these follow-up surgeries should ideally take place approximately 4 weeks after the first procedure. Furthermore, the consensus provides detailed protocols for marking the tumor location and selecting the best surgical approach. These consensuses offer a practical framework to improve the safety and effectiveness of treating early colorectal cancer. By standardizing surgical decisions, the consensus aims to help patients achieve better long-term recovery and quality of life.

KEYWORDS Early colorectal cancer; endoscopic resection; additional surgery; risk factors; Chinese expert consensus

Introduction

Colorectal cancer in the early stages is characterized by tumors that are limited to the mucosal or submucosal layers and have not penetrated the muscularis propria. The current therapeutic approaches include endoscopic resection and radical surgical resection[1,2]. Endoscopic treatment is associated with superior postoperative quality of life and diminished adverse event rates compared to radical surgery, making endoscopic treatment the preferred primary therapeutic modality[3,4]. Nevertheless, if pathologic evaluation indicates non-curative resection, supplementary radical surgery becomes necessary. In the clinical setting it is inherently difficult to ascertain the presence of residual cancer or lymph node metastasis solely on the basis of the pathologic assessment of the endoscopically resected specimens[5-7]. Developing an expert consensus on the diagnosis and treatment

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Received December 5, 2025; accepted January 23, 2026;
published online March 18, 2026.
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of non-curative endoscopic resection and subsequent surgery for early colorectal cancer is clinically important to address clinical imperatives and integrate novel concepts, technologies, and experiences into the management of colorectal cancer.

Methods

The following groups commissioned the consensus and designated Professors Zhongtao Zhang and Guiying Wang as the guideline leaders, who subsequently extended invitations to the listed authors to partake in the creation of the consensus:

- Colorectal Tumor Integrated Rehabilitation Professional Committee, China Anti-Cancer Association
- Digestive Tract Polyp and Precancerous Lesion Professional Committee, Chinese Anti-Cancer Association
- Colorectal Surgery Group, Society of Surgery, Chinese Medical Association
- Colorectal Group, Society of Digestive Endoscopy, Chinese Medical Association
- Surgical Group, Colorectal Tumor Committee, Chinese Medical Doctor Association.

The coordinating team was responsible for formulating the key questions, which were subsequently endorsed by the remaining members. The team established two task force subgroups (one subgroup specializing in surgical aspects and one subgroup specializing in endoscopic procedures) led by Professors Qian Liu and Yunshi Zhong, respectively. These subgroups were tasked with dividing the key topics, including pre-treatment evaluation, treatment modalities, and post-treatment management, in February 2024.

Each task force executed a methodical literature search across PubMed, CNKI, and Wanfang Data, concentrating on articles published from January 2010 to February 2024, to establish evidence-based statements. The selection of articles was performed by title with relevance affirmed through manuscript review and significant articles were evaluated and graded individually using the U.S. Preventive Services Task Force (USPSTF) (**Table 1**)[8]. Draft statements formulated by the task forces were deliberated and subjected to voting through an online survey in May 2024. A draft compiled by the leaders and coordinating team underwent further discussion by all members during an offline meeting in November 2024. A statement necessitated a consensus exceeding 80% for endorsement. The Chinese version of the consensus was disseminated in the Chinese Journal of Practical Surgery in April 2025[9].

To foster enhanced exchanges and cooperation with international counterparts, dismantle informational barriers, and elucidate the China' perspectives within this domain, the English translation version of the consensus was submitted to the *Cancer Biology & Medicine*. All contributing authors consented to the final version of the revised manuscript and the accompanying statements (**Table 2** and **Figure 1**).

Recommendations and levels of evidence

Clinical question 1: What endoscopic findings indicate that a lesion may be amenable to endoscopic resection versus requiring surgical intervention? (Figure 2)

Pre-endoscopic evaluation for possible manifestation of submucosal infiltration

Recommendation 1: Colorectal mucosal lesions should be described and reported according to site, size (in mm), and morphology (Paris classification). Laterally spreading tumors

Table 1 Grade definitions of The U.S. Preventive Services Task Force (USPSTF)

Grade	Definition	Suggestions for practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
E	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Table 2 Chinese expert consensus on additional surgery following endoscopic resection for early colorectal cancer (2025 edition). Complete list of statements

Pre-endoscopic evaluation for possible manifestation of submucosal infiltration
Recommendation 1: Colorectal mucosal lesions should be described and reported according to site, size (in mm), and morphology (Paris classification). Laterally spreading tumors should also be categorized into the following types: (a) nodular homogeneous type; (b) nodular mixed type; (c) flat elevated type; and (d) pseudo-depressed type.
Recommendation 2: Endoscopic diagnostic descriptions and reports of colorectal mucosal lesions should include lesion pit pattern and vascular morphology, and should be combined with macroscopic morphology and location to predict the risk of submucosal infiltration.
Recommendation 3: A combination of white-light endoscopy, image-enhanced endoscopy, magnifying endoscopy, and endoscopic ultrasonography is recommended for visualization and evaluation of lesions.
Choice of endoscopic resection method
Recommendation 4: *En bloc* resection, such as endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR), should be considered for sessile or flat lesions if conditions permit. *En bloc* resection should be performed for pedunculated polyps. *En bloc* resection should at least be considered for the nodular components for LSTs if fibrosis is present.
Recommendation 5: Endoscopic biopsy and marking may be considered for lesions with suggestive features of deep submucosal invasion, followed by surgical intervention.
Pathologic evaluation after endoscopic resection
Recommendation 6: Endoscopic whole resection specimens should be processed with full axial extension and pathologic evaluation.
Recommendation 7: The pathology report should include the following information: integrity of the specimen; lesion size; lesion morphology; histologic type; degree of differentiation; extent of infiltration; depth of invasion; mucosal margins; presence of vascular–lymphovascular invasion; and tumor outgrowth. Immunohistochemical markers should be added when necessary. The report should also comment on head invasion or stalk invasion for pedunculated lesions with the distance of the deepest part of the tumor infiltration from the margins indicated.
Indications for additional surgery
Recommendation 8: Additional surgery is recommended following endoscopic resection if any of the following pathologic features are present: histologic features associated with poor prognosis, including poor differentiation (poorly differentiated carcinoma, undifferentiated carcinoma, mucinous adenocarcinoma, or signet-ring cell carcinoma) or lymphovascular or neural invasion; non-*en bloc* resection, fragmented specimens, or unevaluable margins; submucosal invasion depth > 1000 μm; positive resection margin (tumor present < 1 mm from the margin or tumor cells visible at the electrocautery margin); or G2/G3 tumor budding.
Timing of additional surgery
Recommendation 9: The timing of additional surgery following endoscopic resection should comprehensively consider certain factors, such as resolution of edema, ulcer healing, localization of residual tumor, and patient preference. Additional surgeries are suggested to be completed approximately 4 weeks after endoscopic resection.
Pre- or intra-operative tumor localization
Recommendation 10: Preoperative endoscopic localization using dyes, specifically nanocarbon or isosulfan blue, is recommended for lesions above the peritoneal reflection with submucosal multipoint injections around the intestinal circumference. Preoperative endoscopic placement of metal clips that mark the proximal and distal margins is advised for lesions below the peritoneal reflection. Intraoperative colonoscopy and digital rectal examination are suggested as supplementary methods.
Treatment modalities
Recommendation 11: Proximal and distal resection margins ≥ 5 cm from the ulcer edge (scar) are recommended for lesions located in the colon requiring additional surgery. A distal resection margin ≥ 1 cm from the ulcer edge is recommended for rectal lesions. A shorter distal margin may be acceptable for low rectal surgery but intraoperative frozen section analysis of the distal margin is needed to confirm the absence of tumor infiltration.
Recommendation 12: Routine lymph node dissection up to the second station (D2) is recommended for additional surgeries following endoscopic resection. Extension to the third station (D3) should only be performed when imaging or intraoperative exploration reveals enlarged lymph nodes.

Table 2 Continued

Recommendation 13: The risk of residual tumor and lymph node metastasis should be evaluated on the basis of the number of risk factors in low rectal cancer patients for whom anal preservation is challenging. The following treatment options may be adopted alone or in combination after MDT discussion considering the physical condition of the patient and preference for anal preservation on the basis of the Mismatch Repair (MMR) or Microsatellite Instability (MSI) status: adjuvant chemoradiotherapy; watchful waiting; additional radical surgery; or immunotherapy (monotherapy or combined with radiotherapy).
Follow-up
Recommendation 14: Routine follow-up is recommended for patients who undergo additional radical surgery after noncurative endoscopic resection. Increasing the frequency of colonoscopy and MRI in addition to routine follow-up is recommended for patients who do not undergo additional radical surgery.

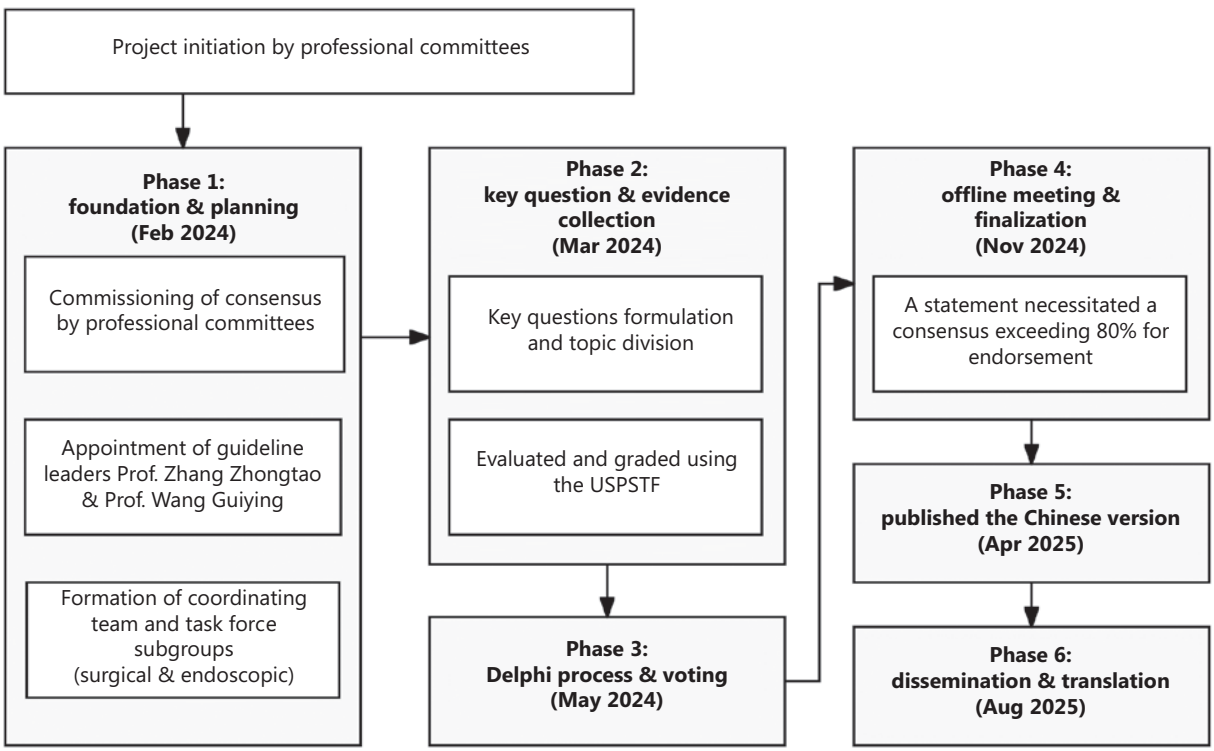


Figure 1 Flowchart of the consensus development process.

should also be categorized into the following types: (a) nodular homogeneous type; (b) nodular mixed type; (c) flat elevated type; and (d) pseudo-depressed type (Strength of Evidence Grade B, High Recommendation).

Recommendation 2: Endoscopic diagnostic descriptions and reports of colorectal mucosal lesions should include lesion pit pattern and vascular morphology, and should be combined with macroscopic morphology and location to predict the risk of submucosal infiltration (Strength of Evidence Grade B, High Recommendation).

Recommendation 3: A combination of white-light endoscopy, image-enhanced endoscopy, magnifying endoscopy, and endoscopic ultrasonography is recommended for visualization and evaluation of lesions (Strength of Evidence Grade B, Moderate Recommendation).

Comments: Colorectal mucosal lesions are described using the Paris classification, categorized as polypoid (type 0–I), superficial (type 0–II), and depressed (type 0–III)[10]. Okamoto et al.[11] defined laterally spreading tumors (LSTs) as lesions that have a diameter ≥ 10 mm, spread laterally along the intestinal

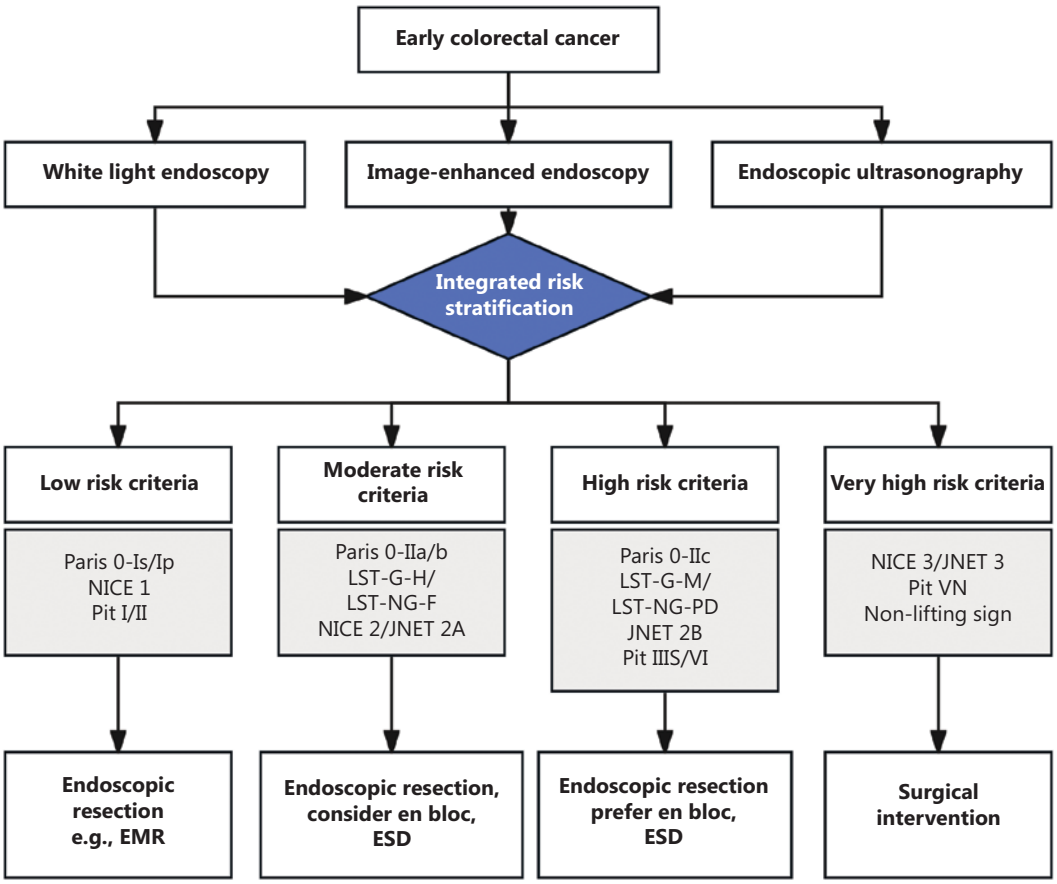


Figure 2 Flowchart of the pre-endoscopic evaluation and choice of endoscopic resection method.

wall, and are classified as Paris type 0–II or 0–I based on the further understanding of lesion morphology and submucosal infiltration risk. LSTs are further classified into granular and non-granular types. Granular LST (LST-G) types can be subdivided by nodular morphology and non-granular LST (LST-NG) types, which have a smooth surface and can be categorized by lesion morphology. Morphologic subclassification of LSTs helps predict the risk of submucosal infiltration and fibrosis with pseudo-depressed LST-NG and nodular mixed LST-G having higher risks[12-14]. Uno et al.[15] described the submucosal lifting sign, in which injected fluid fails to lift the polyp. A negative sign may indicate submucosal infiltration but can also result from fibrosis due to previous biopsy, in which case it a negative sign does not reflect infiltration and is not a contraindication to endoscopic resection[16].

The endoscopic surface morphology of colorectal mucosal lesions is categorized according to several classifications. For image-enhanced non-magnified endoscopic classification, European, American, and Japanese experts proposed the narrow band Imaging (NBI) International Colorectal Endoscopic (NICE) Classification of colorectal polyps in 2010, which can be divided into the following three categories according to color, vascularity, and surface and glandular orifice morphology: NICE type 1 includes hyperplastic polyps or sessile serrated adenomas/polyps (SSAs/Ps); NICE type 2 includes adenomas; and NICE type 3 includes deep submucosal invasive carcinomas[17,18]. Distinguishing low-grade neoplasia, high-grade neoplasia, and superficial submucosal infiltration among NICE type 2 lesions is difficult based on the image-enhanced magnification endoscopic classification. Japanese experts proposed the Japan NBI expert team (JNET) classification in 2016, which is based on polyp performance under NBI magnification endoscopy, surface glandular ductal openings, and microvascular manifestations as follows: type 2A corresponds to low-grade intraepithelial neoplasia; type 2B corresponds to high-grade intraepithelial neoplasia or superficial submucosal invasive carcinoma; and type 3 corresponds to deep submucosal

invasive carcinoma[19,20]. The Kudo classification, which is based on the glandular opening pattern (pit pattern), requires magnifying colonoscopy and dye spraying to evaluate malignant polyps. This method identifies six types; types III–V are considered dysplastic and malignant[21,22].

In summary, pseudo-depressed and nodular mixed LST-G indicate a higher risk of submucosal invasion. Some IIc, IIa + dep, and Is + IIc lesions may also suggest such a risk. NICE type 2 or JNET type 2B endoscopic surface morphology implies superficial submucosal invasion, whereas NICE type 3, JNET type 3, or pit pattern V (VN and VI) suggest deep submucosal invasion.

Choice of endoscopic resection method

Recommendation 4: *En bloc* resection, such as endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR), should be considered for sessile or flat lesions if conditions permit. *En bloc* resection should be performed for pedunculated polyps. *En bloc* resection should at least be considered for the nodular components for LSTs if fibrosis is present (Strength of Evidence Grade C, Low Recommendation).

Recommendation 5: Endoscopic biopsy and marking may be considered for lesions with suggestive features of deep submucosal invasion, followed by surgical intervention (Strength of Evidence Grade B, Moderate Recommendation).

Comments: Endoscopic *en bloc* resection should be considered for accurate pathological evaluation for non-tipped lesions without endoscopic features of deep submucosal infiltration. Depressed (0–IIc) polyps are often related to invasive carcinoma; a study has revealed that 61% of 0–IIc lesions infiltrate the submucosal layer[10]. Burgess et al.[23] reported that 0–Is and 0–IIa+0–Is lesions are more strongly associated with submucosal invasive carcinoma than 0–IIa lesions. The infiltration point is usually below the largest nodule for nodal mixed LST-G and whole-block excision of the largest nodule and suspicious nodules is recommended for better histologic evaluation. Endoscopic features that increase the risk of superficial submucosal infiltration include LST-NG (especially depressed) and LST-G with larger nodules. Accurate measurement of submucosal infiltration depth can be achieved through whole-lesion resection and detailed pathologic diagnosis. Superficial submucosal infiltration has a low risk of residual or lymph node metastasis after endoscopic resection. Thus, surgery can be avoided for whole-excision cases but additional surgical resection is needed after segmental resection.

Surgical procedures are recommended for mucosal lesions with endoscopically observed deep submucosal invasion. A previous study involving stage T1 colorectal tumors has reported that surgical patients have better overall survival than patients who undergo polypectomy[24] with consistent results after adjusting for multiple factors.

Clinical question 2: What pathologic features of a lesion necessitate additional surgical intervention after endoscopic resection? (Figure 3)

Pathologic evaluation after endoscopic resection

Recommendation 6: Endoscopic whole resection specimens should be processed with full axial extension and pathologic evaluation (Strength of Evidence Grade B, High Recommendation).

Recommendation 7: The pathology report should include the following information: integrity of the specimen; lesion size; lesion morphology; histologic type; degree of differentiation; extent of infiltration; depth of invasion; mucosal margins; presence of vascular–lymphovascular invasion; and tumor outgrowth. Immunohistochemical markers should be added when necessary. The report should also comment on head invasion or stalk invasion for pedunculated lesions with the distance of the deepest part of the tumor infiltration from the margins indicated (Strength of Evidence Grade C, Low Recommendation).

Comments: The lesion should be suctioned through the biopsy orifice or removed with a mesh basket or loopers *via* the scope for resected tipped polyps. Large one-piece tipped lesions should not be cut off for suction removal. The lesion specimen should be sent for pathologic examination, during which the lesion is cut in half and the polyp cephalic end and tip are sectioned. Incorrect orientation of the pathologic section may prevent full assessment of lesion residue features, possibly requiring additional surgery. The fresh specimen should be unfolded, secured with staples on a hard flat surface, then immersed in 10% formalin for sessile or flat lesions with suspected submucosal infiltration resected *en bloc* by EMR or ESD; otherwise, contraction and curling will prevent proper orientation and sectioning. Pathologic sections should be perpendicular to the excision plane, usually with a 2-mm interval across the lesion. Poor specimen orientation makes it difficult for pathologists to locate margins, leading to inaccurate infiltration depth measurements and margin involvement assessments[25,26].

A standardized and consistent histopathology reporting system is essential for post-polypectomy decision-making[27]. The College of American Pathologists (CAP) offers an updated template for reporting malignant lesions. The report should list the tumor site and endoscopists should include this and surgery needs in the endoscopic report. Some indicators, such as clusters of poorly differentiated cells of malignant tumors, submucosal infiltration width and area, rupture of cancer glands, and absence of background adenomas, have recently been used to comprehensively reflect the degree of submucosal infiltration. Therefore, units with conditions are recommended to describe and report pathologic findings[28,29]. Standardized pathology diagnosis reports for endoscopic

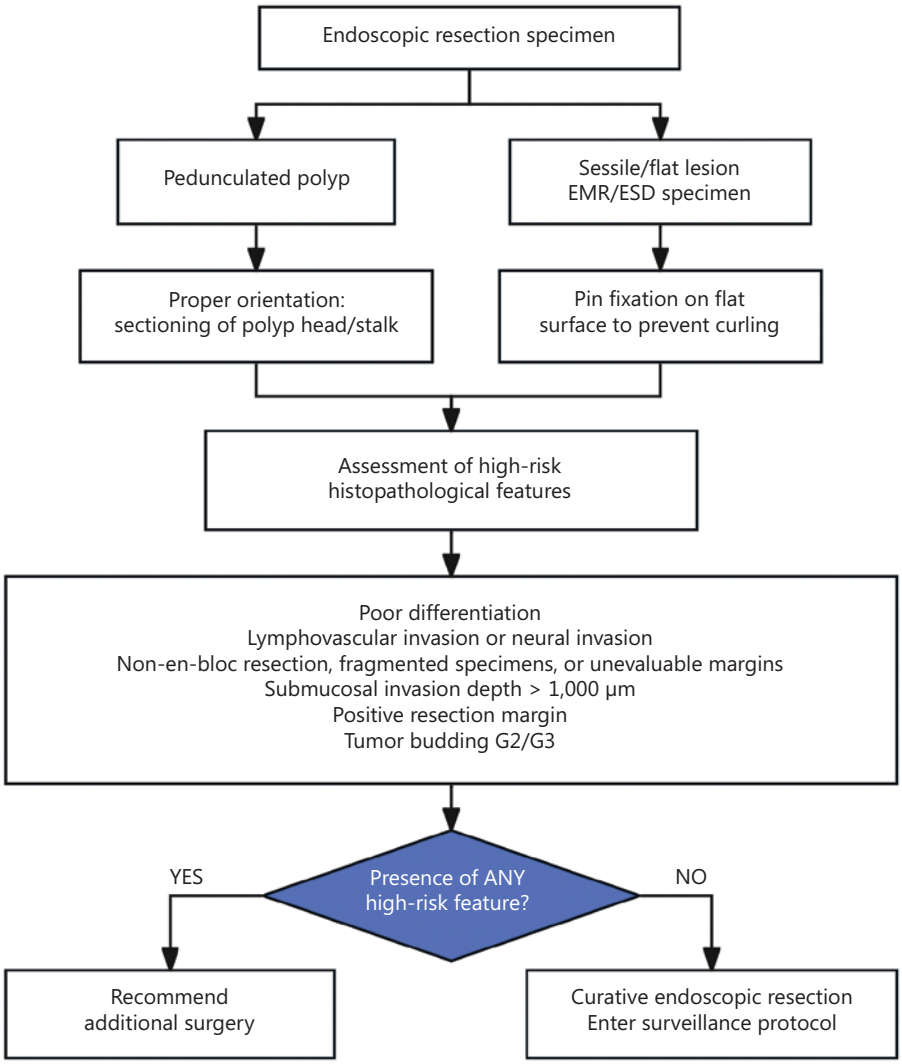


Figure 3 Flowchart of the pathologic evaluation after endoscopic resection and indications for additional surgery.

whole resection specimens should include the following information: (1) basic content, including patient information, specimen and lesion size, horizontal and vertical margins, tumor tissue type, and differentiation grade; (2) submucosal infiltration details, including tissue differentiation type of cancerous tissue, submucosal infiltration depth (using desmin immunohistochemical staining and indicating the measurement method), venous involvement (using elastin fiber staining and D2-40, as well as CD31 immunohistochemical staining), tumor outgrowth grading, and nerve invasion; and if available, (3) clusters of poorly differentiated cells, submucosal infiltration width and area, rupture of cancer glands, and absence of background adenomas.

Indications for additional surgery

Recommendation 8: Additional surgery is recommended following endoscopic resection if any of the following pathologic features are present: histologic features associated with poor prognosis, including poor differentiation (poorly differentiated carcinoma, undifferentiated carcinoma, mucinous adenocarcinoma, or signet-ring cell carcinoma), or lymphovascular or neural invasion; non-*en bloc* resection, fragmented specimens, or unevaluable margins; submucosal invasion depth > 1000 μm; positive resection margin (tumor present < 1 mm from the margin or tumor cells visible at the electrocautery margin); or G2/G3 tumor budding (Strength of Evidence Grade B, Moderate Recommendation).

Comments: Evidence shows that a positive resection margin (cancer tissue < 1 mm from the electrocautery margin) is an independent risk factor for residual tumor and recurrence. In addition, a submucosal invasion depth > 1000 μm, lymphovascular invasion, poor differentiation, and G2/G3 tumor budding are independent risk factors for lymph node metastasis in T1 colorectal tumors[26,30-32]. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines (2024 edition) suggest the need for additional surgery when these factors are present[4]. The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines recommend additional surgery if any of the following four risk factors are present: positive resection margin (< 1 mm or indeterminate); histologic grade III or IV; lymphovascular invasion; or tumor budding[33]. Indications for additional surgical intervention include positive resection margins, deep submucosal invasion, positive lymphovascular invasion, poorly differentiated or undifferentiated carcinomas, mucinous adenocarcinoma, high-grade tumor budding, non-*en bloc* resection, unevaluable margins, and inconclusive pathologic findings in accordance with the Expert consensus on endoscopic diagnosis and treatment for colorectal cancer and precancerous lesions in China (2023, Guangzhou)[34]. National Health Commission guidelines for diagnosis and treatment of colorectal cancer 2023 in China recommend additional segmental resection with regional lymph node dissection for endoscopic resection cases with the following features: histologic features of poor prognosis (poorly differentiated carcinomas with lymphovascular invasion); non-*en bloc* resection, fragmented specimens, or unevaluable margins; submucosal invasion depth ≥ 1000 μm; positive resection margin; and G2/G3 tumor budding[1].

Neural invasion is a high-risk factor for poor prognosis in patients with stage II colorectal cancer but the role as an independent risk factor for poor prognosis in patients with T1 colorectal tumors is controversial. Meta-analysis has shown no significant correlation between neural invasion and prognosis in T1 colorectal cancer[35-38]. However, Rönnow et al.[28] retrospectively analyzed 1439 T1 colorectal cancer patients who underwent radical surgery and reported a significantly increased risk of lymph node metastasis in patients with neural invasion. Therefore, this consensus recommends including neural invasion as an indication for additional surgery.

Clinical question 3: What is the optimal timing and treatment modality for additional surgery? (Figure 4)

Timing of additional surgery

Recommendation 9: The timing of additional surgery following endoscopic resection should comprehensively consider some factors, such as resolution of edema, ulcer healing, localization of residual tumor, and patient preference. Additional surgeries are suggested to be completed approximately 4 weeks after endoscopic resection (Strength of Evidence Grade C, Low Recommendation).

Comments: Currently, there is no consensus on the optimal timing for additional surgical intervention after endoscopic resection of colorectal cancer. Considerations include the risk of lymph node metastasis, surgical technical difficulties due to postinflammatory changes, intraoperative bleeding risk, and patient preferences with an individualized approach for surgical timing. Studies on early gastric cancer have shown that the optimal timing for additional surgery after non-curative resection is approximately 1 month because additional surgery is associated with shorter operative times and lower postoperative complication rates[39,40]. The inflammatory response peaks 1–2 weeks after resection and subsides after 1 month. Resection-site ulceration occurs during the healing or scarring phase at 4–8 weeks and inflammation causes intestinal wall edema and lymph node enlargement[41-43]. The surgical challenges associated with postendoscopic resection inflammatory edema have been significantly reduced with the wide use of minimally invasive techniques, such as laparoscopic surgery. Additional surgeries should be performed promptly based on clinical experience when operational feasibility and patient safety are assured to optimize clinical outcomes. A multidisciplinary team (MDT) approach is recommended considering post-inflammatory surgical difficulty, intraoperative bleeding risk, lymph node metastasis potential from delayed surgery, patient anxiety during waiting, and impact on quality of life[44].

Pre- or intra-operative tumor localization

Recommendation 10: Preoperative endoscopic localization is recommended with the approach tailored to the lesion location: for lesions above the peritoneal reflection, submucosal multipoint injection of dye (nanocarbon or isosulfan blue) around the intestinal circumference is advised; for lesions below the peritoneal reflection, endoscopic placement of metal clips to mark the proximal and distal margins should be performed. Intraoperative colonoscopy and digital rectal examination may be utilized as supplementary localization methods. Preoperative endoscopic placement of metal clips that mark the proximal and distal margins is advised for lesions below the peritoneal reflection. Intraoperative colonoscopy and digital rectal examination are suggested as supplementary methods (Strength of Evidence Grade C, Low Recommendation).

Comments: Endoscopic dye injection is the most widely used method for marking intestinal lesions. The suitable dyes include nanocarbon and isosulfan blue[45,46]. Submucosal injection is recommended to prevent dye leakage and multiple injections around the intestinal circumference are advised for visibility[47-49]. Dye visualization is difficult because of the thick mesorectum for rectal tumors below the peritoneal reflection, which may lead to poor uptake and imprecise localization[50]. In such cases, endoscopic metal clip placement is preferred. Multiple clips enhance accuracy and can be placed proximal and distal to the lesion as needed[51]. Patients should avoid

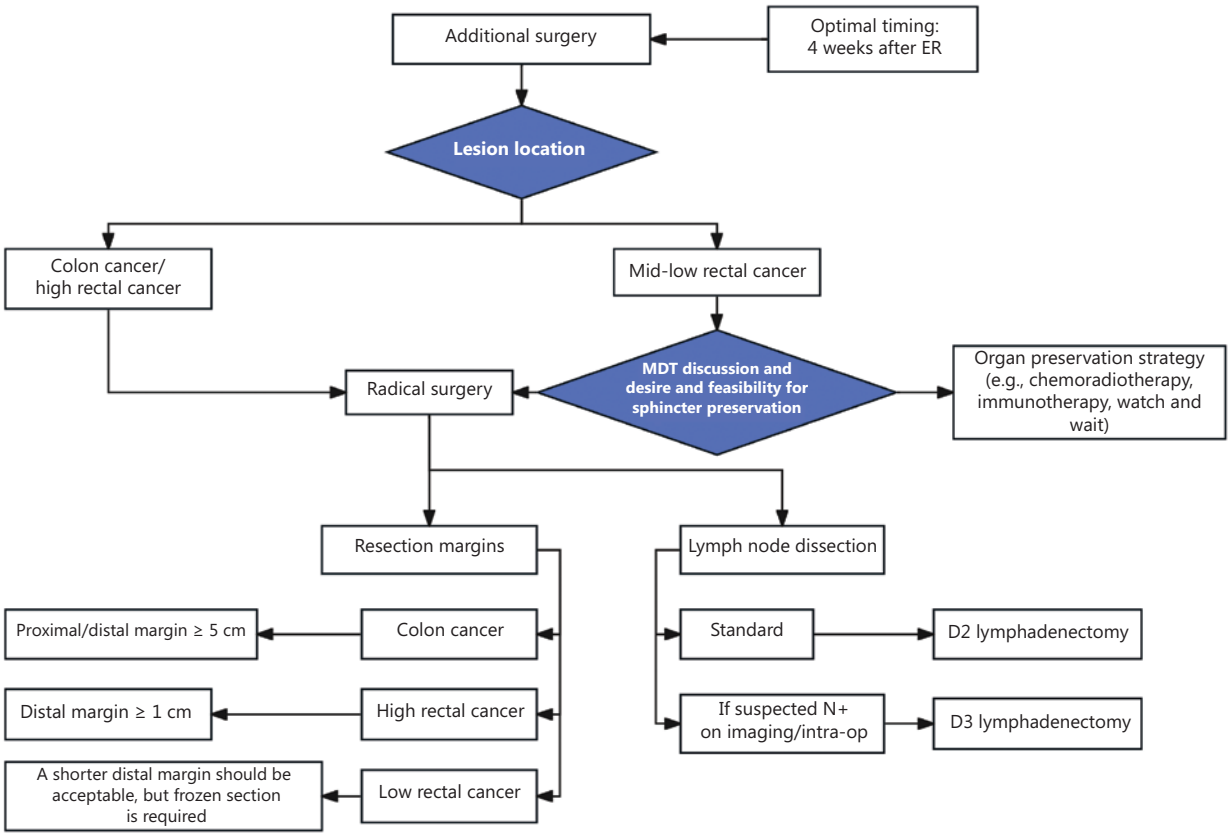


Figure 4 Flowchart of treatment modalities of additional surgery.

vigorous activity and undergo surgery promptly after clip placement. Digital rectal examination or intraoperative colonoscopy can help identify lesions during additional surgeries[36,52,53].

The combination of laparoscopy and colonoscopy is safe and effective for precise localization and can be a salvage method when preoperative localization fails but the clinical application is limited. Residual gas in the intestinal lumen increases surgical difficulty and sterile requirements restrict patient positioning and complicate endoscopic manipulation. In addition, colonoscopy extends the operative time and increases anesthesia risk[54,55].

Determination of resection margins

Recommendation 11: Proximal and distal resection margins ≥ 5 cm from the ulcer edge (scar) are recommended for lesions located in the colon requiring additional surgery. A distal resection margin ≥ 1 cm from the ulcer edge is recommended for rectal lesions. A shorter distal margin may be acceptable for low rectal surgery but intraoperative frozen section analysis of the distal margin is needed to confirm the absence of tumor infiltration (Strength of Evidence Grade C, Moderate Recommendation).

Comments: Anal sphincter preservation is usually not an issue and standard segmental resection for colon cancer can be performed for patients with residual colon lesions after endoscopic resection. Hohenberger et al.[56] reported that ≥ 5 cm proximal and distal resection margins are safe. Only 4–10% of distal bowel wall tumors spread beyond 1 cm from the tumor edge among rectal tumors but the spread of distal mesorectal tumors may reach 3–4 cm beyond the tumor[57,58]. A ≥ 5 cm distal resection margin should be ensured for upper-rectal residual lesions after endoscopic resection. Efforts should be made to preserve the anus to improve postoperative quality of life and the distal margin requirement can be slightly relaxed for mid- or low-rectal lesions, while emphasizing oncologic radicality. A 1-cm distal resection margin may be sufficient when strictly following total mesorectal excision (TME) principles[50,59]. However, multiple methods, such as endoscopic dye injection, titanium clip placement, and digital rectal examination, should assist in pre- and intra-operative localization of the distal edge of the tumor[60-62]. Intraoperative frozen section analysis of the distal margin is recommended to confirm the absence of tumor infiltration. Transanal total mesorectal excision (taTME) enables more precise control of the distal resection margin for low rectal cancer with residual lesions. In addition to the distal margin, achieving an adequate

circumferential resection margin (CRM) is crucial. Entering the correct dissection plane under TME principles generally leads to a low risk of CRM positivity when additional surgery is performed for post-endoscopic resection residual lesions[63].

Lymph node dissection scope in additional surgery

Recommendation 12: Routine lymph node dissection up to the second station (D2) is recommended in additional surgeries following endoscopic resection. Extension to the third station (D3) should only be performed when imaging or intraoperative exploration reveals enlarged lymph nodes (Strength of Evidence Grade B, Moderate Recommendation).

Comments: Studies have reported that the incidence of lymph node metastasis in early colorectal cancer ranges from 6.3–14%[31,50,52]. Recent studies have suggested that the incidence of lymph node metastasis is mainly associated with pathologic features. Risk models for predicting the incidence of lymph node metastasis have been developed on the basis of high-risk factors[36,54]. However, the sensitivity and specificity of these models are suboptimal and lack large-scale, multicenter clinical data validation[55,56]. Preoperative imaging has a limited ability to assess lymph node status and neither the NCCN nor Chinese guidelines offer specific recommendations on the extent of lymph node dissection for early colorectal cancer[1,33,35].

JSCCR guidelines (2024 edition) state that D2 lymph node dissection is sufficient for cT1 colorectal cancer and D3 lymph node dissection is needed if cN(+) is suspected on the basis of Japanese registry data from 2000–2004[4]. A similar Chinese study conducted between 2014 and 2023 has reported low first- and second-station lymph node metastasis rates and no third-station metastases. These findings imply that T1 colorectal tumors rarely metastasize to third-stage lymph nodes and excessive dissection may increase complications and operative time. Therefore, second-station lymph node dissection is adequate in additional surgeries and third-station lymph node dissection should only be performed when metastasis is clearly indicated[64-66].

Treatment strategies for mid-low rectal cancer following non-curative endoscopic resection

Recommendation 13: The risk of residual tumor and lymph node metastasis should be evaluated on the basis of the number of risk factors in low rectal cancer patients for whom anal preservation is challenging. The following treatment options may be adopted alone or in combination after MDT discussion considering the physical condition of the patient and preference for anal preservation on the basis of the Mismatch Repair (MMR) or Microsatellite Instability (MSI) status: adjuvant chemoradiotherapy; watchful waiting; additional radical surgery; or immunotherapy (monotherapy or combined with radiotherapy) (Strength of Evidence Grade C, Low Recommendation).

Comments: Treatment strategies should be chosen carefully considering organ and functional preservation for mid-low rectal cancer after non-curative endoscopic resection; options include additional radical TME surgery, adjuvant chemoradiotherapy, and immunotherapy. Large-scale studies comparing the long-term outcomes of different treatments for high-risk patients after endoscopic resection are lacking. Most studies have shown that adjuvant chemoradiotherapy is less effective than salvage surgery for local control in high-risk rectal cancer patients after local resection. However, a meta-analysis has revealed similar recurrence risks for pT1 tumors between the additional TME surgery and adjuvant chemoradiotherapy groups, as well as a higher risk in the chemoradiotherapy group for pT2 tumors[67].

National Health Commission guidelines for the diagnosis and treatment of colorectal cancer 2023 in China suggest that if radical surgery is not feasible or the patient strongly prefers anal preservation, concurrent chemoradiotherapy followed by watchful waiting can be considered for stage I mid-low rectal cancer with high-risk factors after local resection. Le et al.[68] reported progress in the use of immune checkpoint inhibitors (ICIs) for metastatic colorectal cancer in 2015, starting a new era of immunotherapy. Several studies in 2020, including the KEYNOTE-177 study, revealed that immunotherapy improves prognosis in dMMR/MSI-H metastatic colorectal cancer patients[69]. Therefore, ICIs are recommended as first-line treatment for advanced dMMR/MSI-H colorectal cancer[70].

The NICHE study has reported good results for ICIs in neoadjuvant therapy for patients with initially resectable colorectal cancer. Specifically, among 20 patients with early- to mid-stage dMMR treated with a PD-1 antibody and low-dose CTLA-4 antibody, most achieved good responses with better efficacy than advanced first- or second-line treatments. ICIs have also been shown to be effective in pMMR/Microsatellite Stable (MSS) patients[71]. However, MMR or MSI status is the key marker for predicting immunotherapy efficacy. Owing to the potential toxicity of immunotherapy, strict treatment indications are necessary. PD-1/PD-L1 therapy followed by watchful waiting can be considered for mid-low rectal cancer dMMR/MSI-H patients after non-curative resection with MDT discussion and patient communication.

Clinical question 4: What is the follow-up strategy of additional surgery? (Figure 5)

Recommendation 14: Routine follow-up is recommended for patients who undergo additional radical surgery after non-curative endoscopic resection. Increasing the frequency of colonoscopy and MRI in addition to routine follow-up is recommended for patients who do not undergo additional radical surgery (Strength of Evidence Grade C, Low Recommendation).

Comments: The follow-up strategy for early colorectal cancer after non-curative endoscopic resection followed by additional surgery can align with standard postoperative follow-up

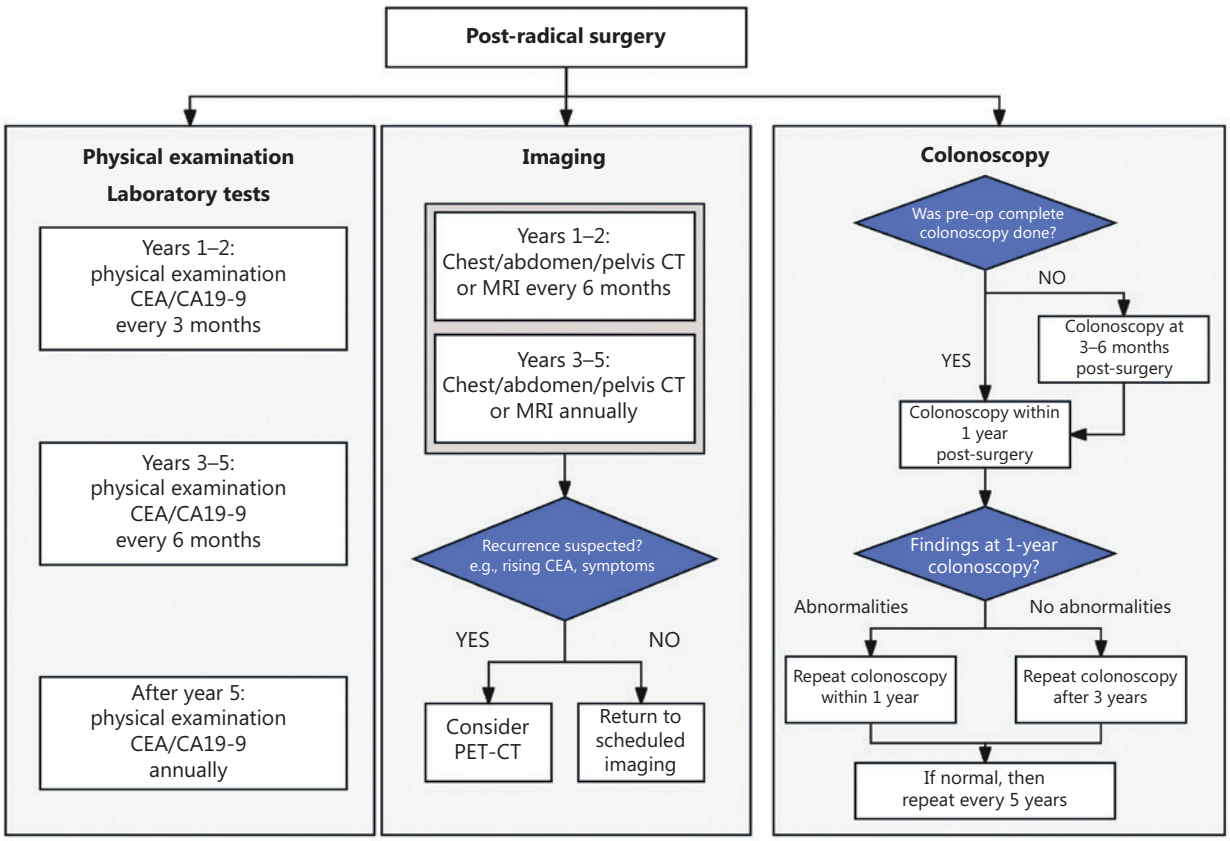


Figure 5 Flowchart of the follow-up strategy for additional surgery.

protocols for colorectal cancer. The follow-up should include the following routines for patients who undergo radical surgery:

1. **Physical examination**: should be performed every 3 months for the first 2 years post-surgery, every 6 months for the next 3 years (up to year 5), and annually thereafter.
2. **Laboratory tests**: should include monitoring of carcinoembryonic antigen (CEA) and CA19-9 levels every 3 months for the first 2 years, every 6 months for the next 3 years, and annually after 5 years.
3. **Imaging**: should include chest, abdominal, and pelvic CT or MRI every 6 months for the first 2 years, then annually for the next 3 years[72,73]. PET-CT may be performed for patients with recurrence or suspected distant metastasis.
4. **Colonoscopy**: should be performed within 1 year post-surgery. If abnormalities are detected, a colonoscopy should be repeated within 1 year; if no abnormalities are detected, a colonoscopy should be repeated after 3 years, then every 5 years thereafter.

A colonoscopy should be conducted 3–6 months post-surgery if a complete colon examination was not performed preoperatively.

The NCCN and American Society of Clinical Oncology (ASCO) guidelines recommend the addition of rectosigmoidoscopy (combined with endoscopic ultrasound or pelvic MRI) to the standard follow-up protocol for patients who do not undergo radical surgery[33,74].

Summary

On the basis of a recent literature review, this expert consensus outlines diagnostic and therapeutic strategies for additional surgery after non-curative endoscopic resection of early colorectal cancer. This consensus covers various aspects, such as the endoscopic classification of colorectal lesions, treatment options, specimen evaluation, additional surgery indications, timing, tumor localization, surgical approaches, and follow-up care. These recommendations provide a reference for the standardized management of early colorectal cancer patients. While summarizing current practices, the consensus admits

insufficient evidence-based medical data for some clinical issues, limiting definitive guidance. Thus, future high-quality clinical trials are needed to validate and refine these strategies for more precise and effective patient treatments.

Conflict of interest statement

No potential conflicts of interest are disclosed.

Author contributions

Conceived and designed the analysis: Yunshi Zhong, Qian Liu, Zhongtao Zhang, Guiying Wang.
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Performed the analysis: Yunshi Zhong, Qian Liu.
Wrote the paper: Zhipeng Qi, Fuqiang Zhao, Xuhua Hu.

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Cite this article as: Qi Z, Zhao F, Hu X, Zhong Y, Liu Q, Zhang Z, et al. Chinese expert consensus on additional surgery following endoscopic resection for early colorectal cancer (2025 edition). Cancer Biol Med. 2026; 23: 796-809. doi: 10.20892/j.issn.2095-3941.2025.0784