Emerging endoscopic resection strategies for organ preservation in early colorectal cancer

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Abstract

The management of early colorectal cancer (CRC) is increasingly debated among gastroenterologists and colorectal surgeons, driven by advances in endoscopic resection that enable curative organ-preserving treatment. Conventional endoscopic mucosal resection (EMR) remains the first-line small-to-moderate sized superficial lesions, although its application is limited for larger or fibrotic polyps, because of piecemeal resection and higher recurrence rates. Modified EMR techniques, including anchoring, precutting, and underwater EMR, are widely available and achieve superior technical outcomes without compromising safety, thus broadening the indications for endoscopic resection of low-risk neoplastic lesions. Endoscopic submucosal dissection (ESD) allows *en bloc* resection regardless of lesion size, and provides accurate histopathological evaluation even when curative criteria are not met, though its use is constrained by its technical complexity and limited availability. For rectal lesions exhibiting features suggestive of deep submucosal invasion, endoscopic intermuscular dissection may serve as an effective endoscopic therapeutic option, as it extends the resection plane into the intermuscular space, achieving clear vertical margins while facilitating organ preservation. Endoscopic full-thickness resection, alone or combined with EMR/ESD, addresses non-lifting, fibrotic or anatomically challenging lesions throughout the colon. Together, these modalities have reshaped the therapeutic landscape of endoscopy, allowing curative and organ-sparing management of early CRCs. This review summarizes organ-preserving endoscopic approaches for early CRC, and proposes a practical algorithm for technique selection while identifying key evidence gaps and future directions.

Keywords Early colorectal cancer, endoscopic resection techniques, organ preservation, colonoscopy, invasive endoscopy

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Introduction

Colorectal cancer (CRC) represents a major global health burden, being the fourth most frequently diagnosed cancer and the second leading cause of cancer-related death [1,2]. Early diagnosis is critical, enabling curative treatment and improving long-term survival.

Alongside improvements in early detection, the therapeutic options for localized CRC have expanded considerably. Endoscopic resection has evolved from endoscopic mucosal resection (EMR) to advanced variants, such as anchoring (A-EMR), precut (P-EMR), and underwater (U-EMR), offering improved outcomes. The breakthrough in endoscopic management of early CRC has been achieved with endoscopic submucosal dissection (ESD), enabling *en bloc* resection of lesions over 20 mm, and allowing accurate histopathological assessment for both therapeutic resection and excisional biopsy [3-5]. More recent developments include endoscopic intermuscular dissection, permitting resection within the *muscularis propria* for rectal lesions and Endoscopic full-thickness resection (EFTR), an alternative approach for lesions with deep invasion or significant fibrosis that are not amenable to other techniques [6-8].

These advances offer an alternative to radical surgery, improving complete resection rates, reducing recurrence, and expanding eligibility for minimally invasive endoscopic therapy. The choice between endoscopic and surgical management is based on histopathological risk stratification, and lesions exceeding high-risk criteria require surgical resection, with or without chemoradiotherapy, which remains the gold standard for oncologic control [4,9-11].

In rectal cancer, organ preservation has become a key therapeutic objective. Early rectal tumors can be treated by local excision using surgical or endoscopic techniques. Although transanal minimally invasive surgical approaches enable full-thickness resection, their application is limited for tumors larger than 3 cm or involving the dentate line, and may compromise subsequent radical surgery if needed [12,13]. In contrast, advanced endoscopic techniques support organ preservation, and may be curative in carefully selected early cancers, or can be integrated into multimodal strategies, while preserving the option for effective salvage surgery [14-16]. The purpose of this review is to provide an overview of the available endoscopic resection strategies for early CRC management, with an emphasis on organ preservation, to propose a practical algorithm for technique selection based on lesion characteristics, and to critically appraise the current evidence in order to identify knowledge gaps and highlight future research perspectives.

Materials and methods

A literature search of the MEDLINE electronic database was conducted from database inception up to February 2026. The search was limited to human studies and articles published in the English language. The search terms included the following, both as Medical Subject Headings and as free-text terms: "Early colorectal cancer", "Colorectal neoplasia", "Endoscopic resection", "Endoscopic mucosal resection", "Conventional endoscopic mucosal resection", "Anchoring endoscopic mucosal resection", "Tip-in endoscopic mucosal resection", "Precutting endoscopic mucosal resection", "Endoscopic mucosal resection with circumferential incision", "Knife-assisted snare resection", "Underwater endoscopic mucosal resection", "Underwater injection endoscopic mucosal resection", "Band ligation-assisted endoscopic mucosal resection", "Cap-assisted endoscopic mucosal resection", "Endoscopic submucosal dissection", "Endoscopic intermuscular dissection", "Endoscopic full-thickness resection", "Hybrid endoscopic full thickness resection", "Organ preservation", "Robotic endoscopy, Artificial intelligence". Randomized or non-randomized clinical trials, observational studies, systematic reviews, meta-analyses, case series and published international guidelines by societies were included. Exclusion criteria included non-human, *ex vivo* or pilot studies, conference abstracts, editorials and case reports.

The PICO (Patients, Intervention, Comparison, and Outcome) framework was used for screening the database. Eligible patients (P) were adults (18-years old) with early CRC. The intervention (I) had to be an endoscopic resection method for removal of colorectal neoplastic lesions. Included studies should compare (C) standard or alternative endoscopic resection techniques. However, studies investigating the feasibility, the safety profile and the recurrence after resection in general, without comparison groups, were also included. The primary outcomes (O) were *en bloc* resection rates, R0 resection rates, recurrence rates, procedural time and complication rates. Articles were individually screened for inclusion and selected by 2 authors (MS and AP).

Endoscopic techniques

Conventional EMR (c-EMR)

EMR constitutes a well-established technique commonly chosen as a minimally invasive endoscopic treatment for colorectal polyps and early CRC [17,18]. International guidelines suggest EMR as the gold-standard technique for the management of non-pedunculated lesions larger than 20 mm [19,20]. However, c-EMR can also result in higher R0 resection rates among neoplastic colorectal lesions sized <10 mm [21]. The majority of studies focusing on EMR for the treatment of early CRC include lesions with high grade dysplasia (HGD), intramucosal cancer (pTis), or superficial submucosal cancer (pT1). For these early-stage cancerous lesions, achieving *en bloc* resection is fundamental for both accurate histopathological evaluation and definitive treatment [22].

Previous studies have revealed that among colorectal laterally spreading tumors (LST) measuring above 20 mm, c-EMR presents a significant risk of piecemeal resection and a higher risk of residual disease [23,24] (Table 1). Namely, among colorectal lesions larger than 10 mm, c-EMR fails to achieve *en bloc* resection in approximately 2% to 30% of cases [23,25,26]. The mean recurrence risk after c-EMR is estimated at 15%, while the recurrence rate is higher after piecemeal resection (20%) compared to *en bloc* resection (3%; P<0.001) [27]. Thermal ablation of the post-EMR mucosal defect margins reduces recurrence at 6-month surveillance endoscopy from 21% to 5%, thereby eliminating lesion size as an independent predictor of recurrence following EMR of large non-pedunculated colorectal polyps [28,29]. Furthermore, thermal ablation of the resection base has been shown to further reduce recurrence rates to approximately 1% [30,31].

EMR may result in post-procedural bleeding, particularly following resection of larger lesions, with reported rates of 5-10% for lesions exceeding 20 mm [19]. The perforation rate is estimated to range from 0.8-3.0%; however, it is lower compared to ESD, hybrid or precut EMR methods [32]. In addition, the risk of significant thermal injury during c-EMR is reduced because of the submucosal injection, while the

Table 1 Main procedural outcomes of endoscopic techniques

Author [ref.], Date	Study	Sample	Location	Techniques	*En bloc* rate	Complete resection rate	A.E. (%)	R.R. (%)
McKechnie *et al* [112], 2022	Systematic review & meta-analysis	1551 procedures	Colon & Rectum	EFTR	89% (95%CI 87-92%)	79% (95%CI 76-82%)	Perforation 2% (95%CI 1-2%). Bleeding 5% (95%CI 3-7%).	7.3% for lesions vs. 6.4% for adenocarcinoma
Zwager *et al* [111], 2020	Prospective	367 procedures	Colon & Rectum	EFTR	83.9%	82.4%	9.3% (2.7% severe - mostly perforations)	6.4%
Moons *et al* [6], 2022	Prospective	67 patients	Rectum	EID	96% (95%CI 89-99%)	81% (95%CI 70-89%)	12% (minor adverse events)	N/A
van Eijck van Heslinga *et al* [83], 2025	Retrospective	1202 lesions	Colon & Rectum	ESD	90.5% for superficial-SMIC vs. 61.9% for suspected deep SMIC	90.6% for superficial-SMIC vs. 55.4% for suspected deep SMIC	3.6% sSMIC vs. 5.8% dSMIC	N/A
Okumura *et al* [80], 2023	Retrospective	1344 patients, 1539 lesions	Colon & Rectum	ESD	98.6%	97.2%	Perforation 2.8% and Bleeding 1.4%	0.5%
Fleischmann *et al* [5], 2021	Retrospective	1000 lesions	Colon & Rectum	ESD	92.4% (95%CI 0.90-0.94)	78.8% (95%CI 0.76-0.81)	8,3% (95%CI 0.69-0.75)	2.1%
Rönnow *et al* [81], 2018	Retrospective	301 lesions	Colon & Rectum	ESD	80%	69%	8%	3%
Singh *et al* [90], 2023	Systematic review & meta-analysis	4206 patients	Colon & Rectum	ESD	84.6% (83.3-85.9%)	75.6% (74.1-77%)	Post op perforation: 5.5% (4.2-7%). Bleeding 4.1% (3-5.5%)	N/A
Ohata *et al* [77], 2022	Prospective	1740 patients, 1814 lesions	Colon & Rectum	ESD	97%	90.4%	Post-op perforation: 0.57%.	0.5% at 3 years and 1.6% at 5 years
Arezzo *et al* [91], 2016	Systematic review & meta-analysis	4678 patients	Colon & Rectum	ESD vs. EMR	89.9% (ESD) vs. 34.9% (EMR) RR 1.93, 95%CI 1.46–2.54; P<0.001	79.6% (ESD) vs. 36.2% (EMR) RR 2.01, 95%CI 1.76–2.29; *P*<0.001	Post-op perforation: 4.9% (ESD) vs. 0.9% (EMR) RR 3.19, 95%CI 2.14–4.77; P<0.001 Bleeding 1.9% (ESD) vs. 2.9% (EMR) RR 0.68, 95%CI 0.44–1.03; *P*=0.07	0.7% (ESD) vs. 12.7% (EMR)
Niu *et al* [36], 2023	Systematic review & meta-analysis	1244 lesions	Colon & Rectum	Tip- in EMR vs. c-EMR	OR 3.61, 95%CI 2.09-6.23; P<0.001	OR 2.49, 95%CI 1.65-3.76; P<0.001	No significant difference	N/A
Takada *et al* [37], 2022	Retrospective	709 lesions	Colon & Rectum	Tip- in EMR vs. ESD	85.0% vs. 99.3%, P<0.001	62.9% vs. 90.7%, P<0.001	Significantly higher rate of electrocoagulation syndrome in the ESD group (0% vs. 5.0% P=0.022)	No significant difference

(*Cond...*)

Table 1 (*Continued*)

Author [ref.], Date	Study	Sample	Location	Techniques	*En bloc* rate	Complete resection rate	A.E. (%)	R.R. (%)
Fakhoury *et al* [116], 2024	Systematic review & meta-analysis	244 patients	Colon & Rectum	Hybrid eFTR+EMR	97% (95%CI 88%-100%)	95% (95%CI 90%-99%)	2% (95%CI 0%-5%)	6% (95%CI 2%-12%)
Chen *et al* [55], 2025	Systematic review & meta-analysis	1374 lesions	Colon & Rectum	PEMR vs. c-EMR	OR 3.05, 95%CI 1.83-5.08	OR 1.72, 95%CI 1.03-2.88	Perforation OR 3.25, 95%CI 1.21-8.78	No significant difference
Li *et al* [63], 2021	Systematic review & meta-analysis	759 patients, 893 lesions	Colon & Rectum	U-EMR vs. c-EMR	OR 1.61, 95%CI 1.02-2.53; P=0.04	N/A	No significant difference	OR 0.18, 95%CI 0.07-0.46; P<0.001
De Souza *et al* [65], 2023	Systematic review & meta-analysis	916 lesions	Colon & Rectum	U-EMR vs. c-EMR	OR 1.54, 95%CI 1.15-2.07; P=0.004 comparable rates in polyps≥20 mm	No significant difference	No significant difference	OR 0.56, 95%CI 0.32-0.97; P=0.04
Wang *et al* [56], 2024	Systematic review & meta-analysis	1,727 lesions	Colon & Rectum	U-EMR vs. c-EMR	OR 1.69, 95%CI 1.36-2.10; P<0.001	OR 1.52, 95%CI 1.14-2.03; P=0.004	No significant difference	OR 0.52, 95%CI 0.33-0.83; P=0.006
Tziatzios *et al* [64], 2021	Meta-analysis	1157 procedures	Colon & Rectum	U-EMR vs. c-EMR	RR (95%CI) 1.26 (1.01-1.58); P<0.001	No significant difference	No significant difference	RR (95%CI) 0.52 (0.28-0.94); P=0.03
Tziatzios *et al* [62], 2023	Systematic review and network meta-analysis	5219 procedures	Colon & Rectum	c-EMR, CSP, HSP, CS-EMR, U-EMR	U-EMR was superior to EMR (RR 1.22, 1.09-1.36; P<0.001) U-EMR was now the highest-ranking modality (SUCRA-score 0.86), followed by EMR (SUCRA-score 0.83)	EMR significantly outperformed CSP: RR 1.04 (95%CI 1.00-1.07) EMR was superior to HSP: RR 1.04 (95%CI 1.00-1.08) EMR achieved the highest ranking (SUCRA-score 0.81), followed by CS-EMR (SUCRA-score 0.76)	CSP had significantly fewer overall A.E. compared to HSP (RR 0.78; 0.60-1.01)	N/A

A.E., adverse events; R.R., recurrence rate; ESD, endoscopic submucosal dissection; RCT, randomized clinical trial; eFTR, endoscopic full-thickness resection; EMR, endoscopic mucosal resection, CSP, cold-snare polypectomy; HSP, hot-snare polypectomy; c-EMR, conventional EMR; U-EMR, underwater EMR; CS-EMR, cold-snare EMR; OR, odds ratio; MD, mean difference; CI, confidence interval; N/A, not available; SMIC, submucosal invasive cancer; sSMIC, superficial SMIC; dSMIC, deep SMIC; P-EMR, precutting EMR incidence of post-polypectomy syndrome is calculated to be around 1% [33].

A-EMR/Tip-in EMR

Tip-in EMR, also referred to as A-EMR or anchored snare tip EMR, constitutes a modified EMR technique that facilitates *en bloc* resection of colorectal lesions larger than 20 mm or very flat lesions, in which snare fixation is difficult and the risk of perforation is increased (Table 2) [34]. According to Sato *et al*, A-EMR is associated with significantly higher *en bloc* resection rates compared to c-EMR (90.7% vs. 69.8%, P=0.008) for colorectal sessile polyps larger than 20 mm, including lesions with mucosal or Sm1 invasive cancer [35]. A-EMR is also associated with a significantly higher complete resection rate (odds ratio [OR] 2.49, 95% confidence interval 1.65-3.76, P<0.001) compared to c-EMR, despite a similar procedural duration [36]. Compared to ESD, A-EMR results in significantly lower rates of *en bloc* resection (85.0% vs. 99.3%, P<0.001) and R0 resection rates (62.9% vs. 90.7%, P<0.001) for large non-pedunculated colorectal neoplasms sized between 20 and 30 mm (Table 1) [37].

Adverse events associated with A-EMR include intraprocedural and delayed bleeding, perforation, deep thermal injury and post-polypectomy electrocoagulation syndrome. Intraprocedural perforation can be mitigated by ensuring adequate submucosal fluid injection and limiting the maximum mucosal incision length of the snare tip to 2 mm. There are no differences in the rates of procedure-related complications between A-EMR and c-EMR or ESD [36,37]. With respect to follow-up outcomes, local recurrence rates after 6 months are also similar between A-EMR and c-EMR or ESD [35,37].

Cap-assisted EMR

Cap-assisted EMR constitutes another modified EMR technique that improves visualization and access to difficult colonic locations, such as the ileocecal valve [38]. Cap-assisted EMR has been used for large (≥20 mm) non-pedunculated colorectal lesions and for fibrotic lesions, as well as salvage treatment after unsuccessful piecemeal wide-field EMR for challenging colorectal LSTs. However, cap-assisted EMR is associated with a significant risk of perforation and bleeding and higher recurrence rates have been reported when argon plasma coagulation of the defect margins is not performed [39,40].

Band ligation-assisted EMR/EMR with a ligation device

Another similar EMR variant that also uses the suction technique followed by mechanical ligation is the band ligation-assisted endoscopic (sub)mucosal resection [41]. It is performed in the rectum, particularly for rectal lesions below the peritoneal reflection, allowing *en bloc* resection. It is indicated as an effective and safe treatment for rectal neuroendocrine tumors sized ≤10 mm, with high R0 resection rates (89-99%) and minimum recurrence rates among lesions with no lymphovascular invasion [42,43]. It demonstrates higher complete resection rates than c-EMR (93.3% vs. 65.5%, P=0.001) and outcomes comparable to ESD [44,45]. However, its use is limited for lesions ≤10 mm in the rectum.

P-EMR/EMR with circumferential incision/Knife-assisted snare resection EMR

EMR with circumferential incision, or P-EMR, or knife-assisted snare resection EMR constitutes an altered EMR technique that involves a circumferential incision using a snare tip or an ESD knife, followed by snaring (Table 2) [46-48]. P-EMR is ideally used for colorectal serrated lesions sized from 20-30 mm and for lesions larger than 20 mm with inadequate submucosal lifting due to fibrosis or a difficult location. It is not recommended for lesions larger than 30 mm and should be performed by experienced endoscopists, as it entails a higher risk of perforation [49-51]. Although more time-consuming than c-EMR, P-EMR has shorter procedural times than ESD [47,52].

According to a meta-analysis of 12 studies, including 2575 lesions sized 10-30 mm, P-EMR achieved significantly higher *en bloc* and R0 resection rates compared to c-EMR, particularly for sessile lesions of the Right colon. However, compared to ESD, P-EMR resulted in lower *en bloc* resection rates (relative risk 0.85, P=0.02) but similar R0 resection rates [53]. Jung *et al* compared P-EMR, c-EMR and ESD among colorectal LSTs with exclusively advanced histology, and revealed that perforation rate was significantly higher in the P-EMR group [54]. Similarly, a meta-analysis of 7 studies revealed that P-EMR is associated with a greater perforation risk compared to c-EMR [55]. In contrast, Chinzon *et al*, in a meta-analysis of 8 studies, demonstrated a statistically significant higher perforation rate with the ESD technique vs. P-EMR. Concerning recurrence rates, P-EMR results in a lower risk of recurrence compared to c-EMR, while there is no statistically significant difference between P-EMR and ESD (Table 1) [53].

U-EMR/Underwater injection EMR

U-EMR technique has emerged as an alternative to c-EMR for the treatment of colorectal lesions, including early CRC. U-EMR has been associated with a shorter procedural time, better visualization, minimization of the risks related to submucosal injection—including perforation, dysplastic seeding and lesion displacement—less diathermy-induced mucosal injury and better procedural tolerability (Table 2) [56-58].

Although classic U-EMR does not include submucosal lift, the submucosal injection can be considered for lesions with larger diameter, polyps spreading above mucosal folds, recurrent or depressed lesions and difficult-to-access colonic

Table 2 Indications, advantages and limitations for each endoscopic technique

Technique	Technique description	Indications	Advantages	Limitations
Conventional EMR (c-EMR)	Submucosal injection to create a mucosal lift followed by snare resection using electrocautery	Non-pedunculated colorectal lesions, <20 mm without suspected deep invasion; adenomas, HGD, pTis, superficial pT1	Widely available; technically straightforward; short procedure time; low complication risk; low cost	High piecemeal resection rates for lesions>20 mm; higher recurrence; limited histological assessment if piecemeal
Anchoring/Tip-in EMR (A-EMR)	After submucosal injection, a small spot-shaped mucosal incision is made with the snare tip to anchor it before closing the snare around the lesion	Flat/LST≥20 mm lesions; lesions with snare slippage; difficult *en bloc* capture	Higher *en bloc* and complete resection rates than c-EMR; good safety profile	*En bloc* and R0 rates remain inferior to ESD; limited evidence; increased perforation risk
Cap-assisted EMR	Snaring performed after suction of the lesion into a transparent cap mounted on the endoscope tip, with or without submucosal injection	Difficult locations (e.g. ileocecal valve); fibrotic or residual lesions; salvage after incomplete EMR	Better visualization and access; useful in anatomically challenging sites or fibrotic lesions	Increased risk of perforation and intraprocedural bleeding; higher recurrence without margin ablation
Band ligation-assisted EMR (EMR-L/ESMR-L)	Lesion is suctioned into a ligation cap, banded, and subsequently resected with a snare after submucosal injection	Small rectal lesions (≤10 mm); rectal neuroendocrine tumors	Very high *en bloc* and R0 resection rates; simple technique; outcomes comparable to ESD for small rectal NETs	Not suitable for larger lesions (>10 mm)
P-EMR/EMR-CI/KAR EMR	Circumferential mucosal incision using snare tip or ESD knife followed by snare resection; incision acts as anchoring groove	Serrated or fibrotic lesions 20-30 mm; non-lifting lesions; right-sided sessile lesions	Higher *en bloc* and R0 rates than c-EMR; shorter procedure time than ESD	Higher perforation risk; technically demanding
U-EMR	Resection performed under water without gas insufflation, allowing separation of mucosa/submucosa from *muscularis propria*	Non-pedunculated lesions, mainly <20 mm; selected ≥20 mm lesions	Improved *en bloc* and complete resection rates vs. c-EMR; reduced recurrence; shorter procedure time	Limited vertical margins; caution in suspected deep T1 cancer
Underwater injection EMR (UIEMR)	U-EMR combined with submucosal injection to allow deeper resection and improved vertical margins	Suspected T1 CRC; larger, depressed or difficult-access lesions	Better vertical margins than U-EMR alone; higher *en bloc* rates for early cancer	Limited data; technique not yet standardized
ESD	Direct dissection of the submucosal layer using endoknives	Lesions ≥20 mm; suspected deep submucosal invasion; non-lifting lesions	Highest *en bloc* and R0 resection rates; optimal histopathological assessment; low recurrence	Technically demanding; longer procedure time; requires expertise
Modified/Traction-assisted ESD	Use of traction devices, pocket creation or immersion techniques to improve exposure and stability during ESD	Large, fibrotic or technically difficult lesions	Faster dissection; higher R0 rates; reduced adverse events vs. conventional ESD	Technique selection depends on anatomy and experience; lack of universal standard
EID	Dissection in the intermuscular plane between circular and longitudinal muscle layers of the rectum	Rectal T1 cancer with suspected deep submucosal invasion or severe fibrosis; need clear vertical margin	Enables clear vertical margins; organ-preserving alternative to surgery	Limited to rectum; expert centers only; not suitable for colon
EFTR	Non-exposed full-thickness resection using an over-the-scope clip-mounted device (FTRD) or endoknives	Non-lifting or fibrotic lesions; appendiceal orifice; suspected deeper invasion; lesions <20-25 mm for FTRD	*En bloc* full-thickness resection; simple steps with FTRD;	Size limitation (<20-25 mm) in FTRD; less maneuverability; lower R0 rates for larger lesions; cost
Hybrid EMR/ESD+EFTR	Peripheral lesion reduction by EMR or ESD followed by EFTR of the central fibrotic component	Complex fibrotic lesions >25 mm not amenable to standard techniques	Enables resection of otherwise unresectable lesions; acceptable safety	Limited evidence; EMR+EFTR compromises histology; technically complex

HGD, high-grade dysplasia; pTis, pathologic tumor in situ; pT1, pathologic T1 cancer; LST, laterally spreading tumor; R0, complete resection with negative margins; NETs, neuroendocrine tumors; CRC, colorectal cancer; FTRD, full-thickness resection device; EMR, endoscopic mucosal resection; c-EMR, conventional EMR; A-EMR, anchoring EMR (tip-in EMR); EMRL/ESMRL, band ligationassisted EMR/endoscopic submucosal resection with ligation; PEMR/EMRCI/KAR EMR, precutting EMR/EMR with circumferential incision/knifeassisted resection; U-EMR, underwater EMR; UIEMR, underwater injection EMR; ESD, endoscopic submucosal dissection; EID, endoscopic intermuscular dissection; EFTR, endoscopic fullthickness resection lesions, as it could prevent perforation during U-EMR [58-60]. Moreover, U-EMR without submucosal injection might not potentially provide a sufficient vertical margin for histological evaluation of T1 CRCs, particularly those with deeper invasion. To address this issue, a modified U-EMR method, called underwater injection EMR, incorporates submucosal lift in order to allow deeper resection and sufficient vertical margins, resulting in higher *en bloc* resection rates for T1 colorectal lesions [61]. Nevertheless, more studies exploring the efficacy and safety of this technique for T1 CRC are indispensable.

A network meta-analysis revealed that U-EMR for non-pedunculated colorectal lesions sized from 6-20 mm can result in higher *en bloc* resection rates compared to c-EMR [62]. Two recent meta-analyses also revealed that, compared to c-EMR, U-EMR was associated with significantly higher *en bloc*, R0 and complete resection rates [56,63]. However, concerning complete resection rates, a meta-analysis of 6 randomized controlled trials found no statistical difference between U-EMR and c-EMR, although significant heterogeneity was observed between studies [64]. Souza *et al* also reported no statistical difference in complete resection rates between U-EMR and c-EMR; however, in a subgroup analysis examining *en bloc* resection rates, U-EMR showed a higher rate among lesions <20 mm, with comparable rates among lesions with size ≥20 mm (Table 1) [65]. Regarding possible adverse events, no significant differences have been observed between U-EMR and c-EMR [56,64,65]. Interestingly, at follow up, the U-EMR technique results in significantly lower recurrence and residual adenoma rate when compared to c-EMR (OR 0.18, 95%CI 0.07-0.46; P<0.001) [56,63,64].

ESD

ESD was initially developed to obtain higher quality specimens for histopathological evaluation, and has helped overcome the limitations of conventional EMR, particularly its low *en bloc* resection rates and poor efficacy for non-lifting lesions and lesions larger than 20 mm [66,67]. These limitations hinder accurate histopathological assessment, and are associated with higher local recurrence, often necessitating additional treatment [12,68-72]. Initially introduced for early gastric cancer, ESD has since been applied throughout the gastrointestinal tract. Although Gauci *et al* reported that ESD use in the right colon cannot be justified, given its higher rate of adverse events, van der Voort *et al* supported a morphology-based selection of resection technique [73,74]. Accordingly, European guidelines recommend ESD for colorectal lesions over 20 mm with limited submucosal invasion, or when snare-based resection is not feasible, while Japanese guidelines endorse ESD for early CRC [3,75,76]. ESD has eventually become the cornerstone of endoscopic treatment for early CRC.

Across studies, ESD is an effective minimally invasive treatment for adenomas with HGD, pTis and early CRC, achieving high *en bloc* (91-97%) and R0 (74-93%) resection rates [5,77-85]. These outcomes are influenced by lesion size, location and morphology [5,81]. Curative resection rates have varied by pathology: adenomas/HGD and pTis reported higher rates than T1a cancer (86-87.2%, 86% and 75.4-78%, respectively) [77,79]. High-volume centers, performing more than 40 ESDs annually, demonstrated superior *en bloc* and R0 resection rates, whereas a lower procedural volume was associated with non-curative resection [4,85]. Following curative resection, recurrence rates are low, particularly in Asian cohorts (0.5-2%), while European studies report slightly higher recurrence rates (2-3%) [5,54,77,78,80,81,84,86]. Identified risk factors for recurrence include piecemeal resection, lesion size larger than 40 mm, non-R0 resection, fibrosis and T1b pathology [5,79,80] (Table 1).

ESD is technically demanding, and requires advanced expertise and specialized training for both endoscopists and supporting staff. Apart from the innate difficulty of ESD, other factors leading to failure of *en bloc* and R0 resection are insufficient operator experience, and fibrosis from previous endoscopic resection attempts or radiation therapy (Table 2) [87]. Even in these high-risk cases, where muscle retraction due to fibrosis is observed, endoscopists have proposed adapted ESD techniques to overcome these difficulties, with substantial success rates [88].

Compared with c-EMR, ESD is associated with higher rates of adverse events, with bleeding and perforation being the most frequent complications of ESD [89]. Asian studies report lower adverse events rates (1.1-2.8%), whereas early European studies described higher rates of approximately 8%, primarily bleeding and perforation; however, more recent European studies report rates comparable to Asian cohorts [5,77,78,80-83,90]. Importantly, most ESD-related adverse events are managed endoscopically, with surgical intervention required in less than 0.5% of cases in Asian series, and less than 3% in European studies [77-80,86,90,91].

Different technical modifications of ESD have been developed to improve the efficacy and safety of conventional ESD. Traction-ESD techniques have been developed to address the lack of surgical triangulation. Lifting and flipping the mucosal flap improves exposure of the submucosal plane, and facilitates precise and safe dissection [92]. While gravity-assisted positioning is commonly used to help expose the submucosal plane, dedicated traction devices, classified as external or internal (depending on whether the force that is applied is inside the lumen or outside), are often required, particularly in challenging locations [3]. Implementation of traction methods has been associated with significantly shorter procedure times, higher R0 resection rates, and lower complication and perforation rates [92,93]. Internal traction techniques (S-O clip, rubber band, double clip, etc.) are generally preferred for colonic lesions, although method selection should be individualized based on lesion characteristics, operator experience and method availability [92-95]. The pocket-creation method (PCM-ESD) is another modification used for colorectal lesions that improves scope stability, access angle and maintenance of the submucosal cushion [96]. Meta-analyses demonstrate that PCM-ESD achieves higher *en bloc* and R0 resection rates, shorter procedure times, faster dissection speed and fewer adverse events compared with conventional ESD [97-99].

Immersion-based techniques further refine ESD. The saline immersion/irrigation technique, a PCM-ESD variant, enhances visualization, tissue cooling and lesion lifting by filling the pocket created with saline or water [96]. Underwater ESD (U-ESD) improves visualization through traction and optical magnification in a fluid-filled lumen. Saline is preferred over water, because of its better conductivity and smaller risk of thermal injury, potentially lowering post-endoscopic coagulation syndrome rates [96]. Meta-analysis data indicate that U-ESD reduces procedure time and increases dissection speed, while showing comparable adverse event rates to conventional ESD, and studies support its safe application throughout the colorectum [96,100,101].

Endoscopic intermuscular dissection (EID)

EID is an advanced technique performed in the intermuscular plane between the inner circular and outer longitudinal muscle layers of the rectum, developed for early rectal cancers with suspected deep submucosal invasion (dSMI) or severe fibrosis, where standard ESD may not achieve complete resection and clear vertical margins [102,103]. By enabling complete submucosal layer resection, EID allows optimal histopathological assessment in suspected dSMI. Its use is limited to the rectum, where the thicker muscular layers and the pelvic anatomy permit safe entry into the intermuscular plane, and is performed only in expert centers. In the colon, EID is generally avoided, because of the thinner wall and higher risk of perforation, and current guidelines— European Society of Gastrointestinal Endoscopy (ESGE) and Japanese Society for Cancer of the Colon and Rectum—recommend EFTR or surgery for lesions where dSMI is suspected or submucosal fibrosis is present (Table 2) [3,75].

In a prospective cohort of 67 patients with suspected dSMI rectal cancer, EID achieved a technical success rate of 96%, and R0 resection rates of 91% for pT1 and 90% for dSMI- pT1, with no local recurrence after curative resection over a follow-up period of 10 months, and only minor adverse events in 12% of cases [6]. Subsequent series have confirmed the feasibility and safety of EID as an organ-preserving alternative to radical surgery in selected T1 rectal cancers (Table 1) [104]. In a 3-year follow-up study, locoregional recurrence occurred in 7% of low-risk and 13% of intermediate-risk patients managed with active surveillance, without distant recurrence or cancer-related mortality, supporting EID as a safe organ-preserving option in carefully selected cases [105]. These findings suggest that EID followed by active surveillance may constitute a safe, organ-preserving alternative to radical surgery for selected low- and intermediate-risk rectal deep submucosal invasive cancer cases.

EFTR

EFTR is a minimally invasive technique that was initially developed for the endoscopic resection of gastric submucosal tumors, and was subsequently applied to colorectal lesions not amenable to EMR or ESD [106]. Two approaches have been developed: exposed and non-exposed techniques; in the colon the non-exposed approach is predominantly used [107,108]. Exposed EFTR, derived from ESD, is classified as tunneled or non-tunneled, and involves performing a full thickness resection first, with subsequent closure of the temporary peritoneal exposure using different methods [108,109]. Exposed techniques have more limitations due to the challenging technique, required closure of large defects, and higher risk of peritoneal contamination and tumor cell dissemination [107,110]. In contrast, non-exposed EFTR achieves serosa-to-serosa apposition, after which full-thickness resection is completed with the assistance of a cap-mounted device-clip.

Although limited for lesions up to 2 cm, the resection devices offer easier handling, simple procedural steps, a lower contamination risk and a shorter learning curve [108,109]. This approach is facilitated by the full-thickness resection device (FTRD), a pre-assembled over-the-scope system enabling single-step resection immediately after the deployment of an over-the-scope clip. Indications for EFTR include non-lifting lesions, fibrotic lesions and lesions in anatomically challenging locations (e.g., appendiceal orifice or diverticulum), and subepithelial tumors (Table 2) [111]. While not fully incorporated into American Society for Gastrointestinal Endoscopy, Japan Gastroenterological Endoscopy Society, or ESGE guidelines, recent ESGE polypectomy guidelines propose non-exposed EFTR as an alternative for superficial invasive carcinoma [19]. A meta-analysis including over 1500 patients reported *en bloc* and R0 resection rates of 89% and 79%, respectively, with a 6.4% overall recurrence rate at 12 months and major adverse events in 2.9% of cases, including emergency surgery in 1.9% [112]. A prospective study including T1 CRC cases showed similar outcomes, with *en bloc* and R0 resection rates of 87% and 85.6%, curative resection in 60% and major adverse events in 2.2%, all of which were perforations necessitating surgical intervention. Concerning the efficacy of the method, the recurrence rate was 2-3.1% [113]. The main limitation of FTRD is size, as the device's outer diameter of 21 mm restricts its maneuverability in patients with a narrow lumen or an angled sigmoid, and precludes passage in the presence of stenosis or adhesions. In addition, its use is limited for lesions <20 mm, as R0 resection rates decline for lesions >20 mm [114].

Hybrid EFTR+ESD/EMR

Complex fibrotic colorectal lesions sized above 25 mm could potentially be removed with a combined approach of EFTR and piecemeal EMR or ESD (hybrid EMR+EFTR and hybrid ESD+EFTR) (Table 2) [115]. A meta-analysis of 8 study arms including 244 patients revealed a pooled rate of macroscopic complete resection at approximately 95%, with a free vertical margins resection rate of 88%. Total complication rate was estimated at 2%, while recurrence rate during follow-up was approximately 6% [116].

Hybrid ESD+EFTR, in contrast to the EMR+EFTR method, results in *en bloc* resection of the lesion, allowing complete histological evaluation and tumor staging. In contrast, during EMR+EFTR, piecemeal resection of T1 colorectal lesions could result in further unnecessary surgical treatment [117]. Andrisani *et al*, following a case by Lupu *et al*, described a case series focusing on the ESD+EFTR hybrid technique applied for fibrotic cancerous colorectal lesions, in which they achieved 100% *en bloc* and R0 resection without any complications or recurrence at follow-up [118,119]. Tribonias *et al*, in a retrospective analysis of either EMR+EFTR or ESD+EFTR of colorectal lesions, including 42.9% lesions with T1 carcinoma, reported a 100% rate of complete macroscopic resection (Table 1). Nevertheless, R0 resection rate was evaluated only in 3 cases that were treated with ESD (100% R0 rate), while no recurrent disease was observed at a mean follow-up of 15.4 months [115].

Algorithm for selection of the optimal resection endoscopic technique

Although international guidelines have published algorithms for the optimal endoscopic management of colorectal polyps, based on their morphology, location or size, there is currently no clearly defined therapeutic algorithm that comprehensively incorporates all the endoscopic resection modalities for the management of early CRC. The current guidelines have not taken into account the higher rates of *en bloc* resection achieved with the different EMR variants, nor have they incorporated the endoscopic removal of rectal lesions with deep submucosal invasion, using EID or EFTR techniques instead of surgery [19,20,76]. Although certain techniques, such as EFTR, have clearly defined indications, there are many clinical scenarios that could be treated using multiple endoscopic approaches. Furthermore, the therapeutic strategy may vary, depending on the endoscopist's level of experience with a given technique and the technical resources available. A proposed algorithm based on the considerations outlined above is presented in Fig. 1. The fundamental principles that should underpin any therapeutic algorithm are outlined below and should be applied universally, across all cases of early CRC.

The first step involves obtaining a detailed medical history from the patient, including age, comorbidities, previous polypectomy history at the same site, and current use of anticoagulant or antiplatelet agents. Subsequently, the characterization of the lesion through thorough inspection and optimal optical diagnosis is essential. Optical diagnosis should always include high-definition white-light endoscopy and chromoendoscopy with narrow band imaging (NBI) and/or dye-based techniques, which enhance diagnostic accuracy and estimation of submucosal invasion risk, followed by classification of the lesion according to the Paris, NICE, JNET, Kudo, and LST systems [120-123]. The presence of depression, surface ulceration, fold convergence or loss of vascular pattern facilitates the estimation of invasion depth [124,125]. Apart from the endoscopic assessment of presence of dSMI, a lifting test performed to detect a potential non-lifting sign should be incorporated in the pre-resection endoscopic evaluation, in order to estimate the technical difficulty of the resection [126]. Additional factors to consider include the lesion's anatomical location within the colorectum, its size, and whether it extends across colonic folds, all of which influence the choice of the appropriate endoscopic resection technique. For rectal lesions, magnetic resonance imaging (MRI) can facilitate staging, particularly for gray-zone cases, when optical endoscopic diagnosis does not allow differentiation between superficial and dSMI. For subepithelial tumors, endoscopic ultrasonography (EUS) also provides further information concerning staging, provided that the lesion's location permits its application [127,128]. Special attention should be given to rectal lesions, where EID or EFTR allows deeper resections, and where an organ-preserving strategy should be pursued whenever feasible, provided that strict follow-up protocols involving endoscopy and/or imaging are adhered to [129].

Knowledge gaps and future perspectives

Emerging endoscopic techniques such as ESD, EID and EFTR enable organ-sparing *en bloc* and R0 resection of early CRC. Their broader adoption, however, is limited by their greater technical complexity, prolonged learning curves and strong operator dependence, with superior outcomes reported by experienced endoscopists in high-volume centers [5]. Unequal access across regions further highlights the need for standardized training curricula to improve technical success and global availability [130].

Optical diagnosis enhances lesion characterization and invasion depth prediction, but remains highly dependent on the endoscopist's expertise and training [131]. Artificial intelligence (AI), including computer-aided diagnosis (CADx) systems and novel magnification endoscopic techniques such as endocytoscopy, may improve diagnostic accuracy, particularly among non-expert endoscopists, and can help distinguish early-stage CRC from other premalignant lesions, preventing piecemeal resection of cancerous lesions and subsequent surgical overtreatment [132]. Further development of real time CADx trained on final histopathology, rather than endoscopic images, could improve invasion depth prediction, margin assessment and selection of the appropriate endoscopic technique for *en bloc* resection (ESD vs. EID or EFTR) [133]. Nevertheless, international committees hold conflicting positions on the routine use of AI, and further studies are required to define its true benefit in terms of an optical diagnosis and treatment plan [134].

Conventional imaging modalities, including computed tomography, MRI or EUS, which frequently overstage early CRC, especially rectal cancer, may lead to overtreatment, while inappropriate tissue sampling may result in a delay of treatment [135,136]. Predictive models that guide the selection of the appropriate excision technique, combining optical diagnosis, biopsy histology and imaging, could improve patient selection and guide appropriate excision strategies while minimizing overtreatment with unnecessary surgery.

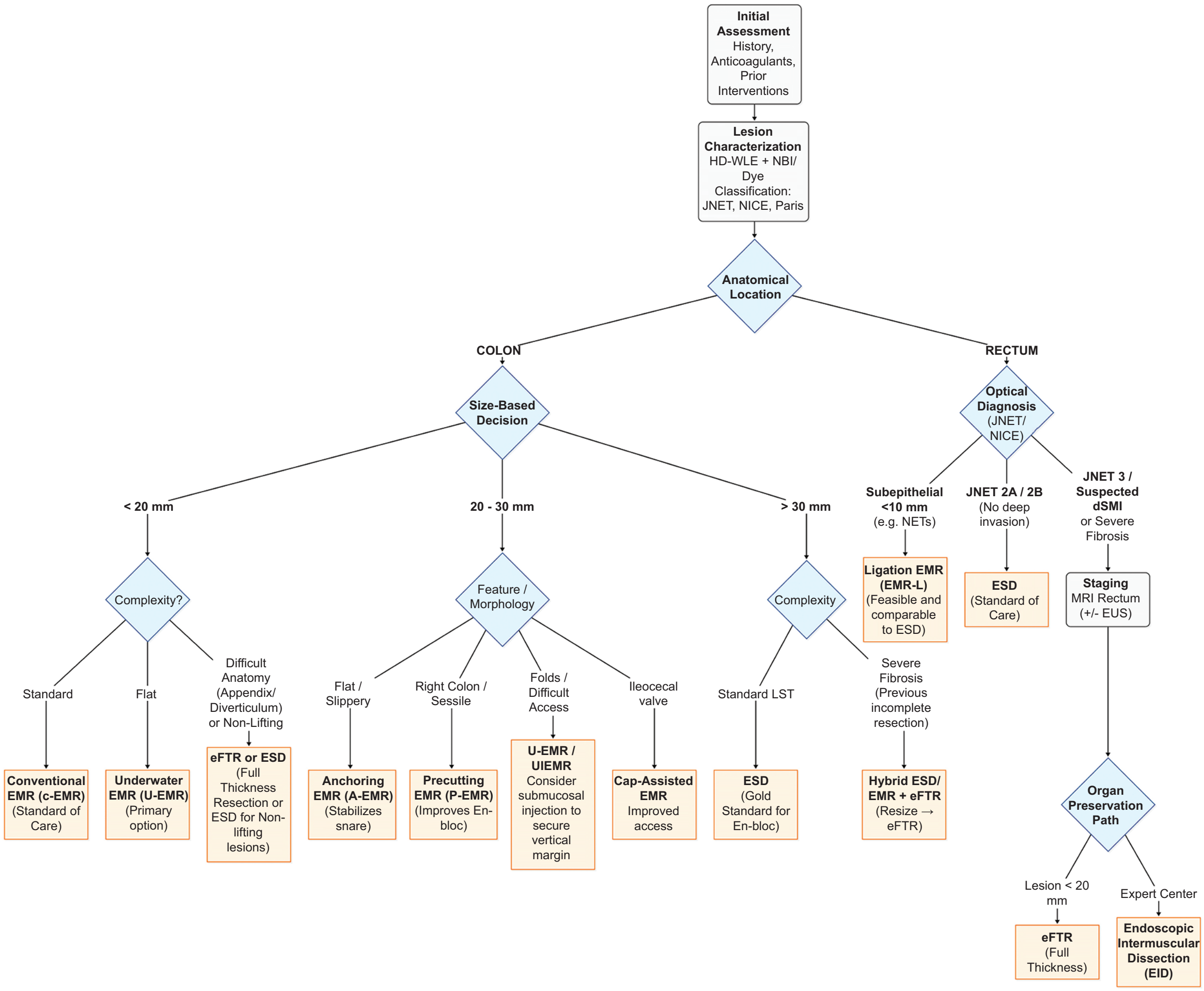

Figure 1 Algorithm for selection of the optimal resection endoscopic technique

For endoscopically resected T1 CRC, significant gaps remain in post-resection management, including surveillance strategies and indications for adjuvant treatment based on margin status and histopathology. Evidence guiding optimal post-ESD surveillance intervals are limited; although international guidelines recommend follow-up colonoscopy at 12 months after curative ESD, data suggest that earlier surveillance colonoscopy is necessary for rectal than for colon cancer [137]. In addition, international guidelines disagree on the definition and management of margin positivity [3,48,138]. The current high-risk pathological features that predict lymph node metastasis (LNM) and further determine the decision for adjuvant treatment with surgery are under question. A recent meta-analysis revealed that deep submucosal invasion alone is a weak independent predictor for LNM, with an absolute LNM risk of 2.6% when present as a solitary risk factor [153]. Further studies are necessary to refine the histopathological predictors of LNM or residual disease, as more than 80% of patients with high-risk features in endoscopic specimens show no residual cancer or LNM after adjuvant surgery [139].

Finally, flexible endoluminal robotic technology is emerging as a novel therapeutic approach for early CRC, addressing key limitations of conventional ESD, such as technical complexity and inadequate tissue traction. In a prospective phase II clinical trial including 43 patients with early CRC, flexible robotic ESD achieved a complete resection rate of 83.8% and an *en bloc* resection rate of 94.6% [140]. Robotic platforms can significantly improve dissection speed, reduce blind dissection by multidirectional traction, and reduce operator workload; however, device size means that its current use is largely limited to the rectosigmoid colon [141]. Further clinical studies are required to better define procedural outcomes and broader applicability.

Therapeutic goals: organ preservation, follow up and quality of life

Surgical resection (SR) remains the standard treatment for early-stage gastrointestinal cancers, as it allows complete tumor and lymph node removal, but it is associated with a high burden of postprocedural adverse events, morbidity and occasional mortality [3,142]. While some studies report higher overall survival (OS) with SR compared to endoscopic resection (ER) for malignant polyps, multiple systematic reviews and cohort studies have shown comparable OS, disease-specific survival, recurrence-free survival and recurrence rates between ER and primary surgery for T1 CRC, including high risk cases, with follow-up up to 5 years [142-145]. Similar results were reported from the GRECCAR2 study of rectal cancer, which showed no difference in the oncological outcome between local excision and surgical excision [146].

Importantly, studies consistently show that, when ER is followed by salvage surgery, oncologic outcomes are not compromised, with similar OS, mortality and local or distant recurrence rates when compared to primary surgery in patients with T1 CRC [3,147-149]. Long-term outcomes, including OS, disease-free survival and recurrence, are also similar between patients managed with surveillance after ER and those who undergo additional surgery [150]. Recurrence rates of T1 CRC after ER range from 3.4-4.6%, compared with 2.3% after surgery, with no differences in metastasis or recurrence between upfront surgery and salvage surgery after ER of pT1SM CRC [48,151,152]. Several studies report favorable outcomes for selected patients with T1 CRC managed with ER and surveillance rather than immediate surgery. Surveillance has been shown to be a viable alternative, even after non-curative resections, with no significant differences in mortality or recurrence, and low recurrence rates over follow-up periods of 44-48 months [153,154]. Furthermore, studies have supported active surveillance, demonstrating low recurrence rates, non-inferior outcomes and high organ preservation rates with effective salvage treatment when needed [18,155]. All these findings support the use of "watch and wait" protocols in selected groups of patients following endoscopic resection of malignant colorectal lesions.

Patient-reported and short-term outcomes consistently favor endoscopic approaches over surgery for early CRC. Endoscopic treatment is associated with faster recovery (by approximately 3 months), better postoperative quality of life, lower symptom burden, shorter hospital stays, and earlier resumption of oral intake, without increased fear of cancer recurrence compared with surgical resection [139,156-158].

Concluding remarks

The evolution of endoscopic resection techniques has redefined the therapeutic landscape of early CRC. EMR and its advanced modifications, ESD, EID, and EFTR collectively allow curative, minimally invasive management for a growing proportion of early lesions that were previously treated surgically. Among these, ESD remains the cornerstone for *en bloc* resection of large or high-risk tumors, while EID and EFTR extend the boundaries of endoscopic resection deeper into the bowel wall, particularly within the rectum. Organ preservation can now be achieved in a plethora of cases, provided that decision making is guided by appropriate case selection, endoscopist's expertise and rigorous histopathological evaluation. As technology, experience and training continue to advance, these endoscopic modalities will further consolidate their role in providing curative and viable solutions in the management of early CRC.

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