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Endoscopic strategies for the management of locally recurrent colorectal adenomas

Tommaso Antenucci[a], Rosario Arena[b]

University of Bologna; University Hospital Arcispedale Sant'Anna of Ferrara, Cona, Emilia-Romagna, Italy

Abstract

Endoscopic resection is the standard approach for removing colorectal adenomas. Despite technical advances, recurrence remains a concern. This unique review explores current endoscopic strategies for the management of local adenoma recurrence, evaluating efficacy, safety and limitations, based on available evidence.

Keywords Cancer, endoscopy, recurrence, resection, polypectomy

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Introduction

Colorectal cancer (CRC) ranks second in cancer-related mortality globally. According to GLOBOCAN 2022, CRC accounted for approximately 1.9 million new cases, representing 9.6% of global incidence [1]. CRC typically evolves from mucosal stem cells in aberrant crypts, through adenomatous stages driven by genetic and epigenetic changes [2]. Screening methods, including fecal tests (fecal occult blood test, fecal immunochemical test) and visualization-based approaches (colonoscopy, sigmoidoscopy, computed tomography colonography), are vital for early detection [3]. Endoscopic resection (ER) of colorectal adenomas has significantly reduced CRC incidence, with one Italian cohort reporting a 66% risk reduction following resection of adenomas ≥5 mm [4]. The European Society of Gastrointestinal Endoscopy (ESGE) 2024 guidelines on polypectomy recommend using cold snare polypectomy for the removal of small polyps (6-9 mm) and hot snare polypectomy (HSP) for the removal of non-pedunculated adenomatous polyps of 10-19 mm in size. Conventional (diathermy-based) endoscopic mucosal resection (EMR) is recommended for large (≥20 mm) non-pedunculated adenomatous polyps (LNPCPs), with endoscopic submucosal dissection (ESD) suggested as an alternative, given its ability to resect large lesions in an *en bloc* fashion [5]. However, all ER techniques bear a certain risk of adenoma recurrence (AR). Colorectal AR (Fig. 1) is defined as histologically or endoscopically confirmed residual adenomatous tissue at a previous resection site, typically detected during follow up. Risk factors include adenoma size, number, high-grade dysplasia, proximal location and piecemeal resection [6-8]. One of the postulated mechanisms of recurrence is that microadenomas are left at the margin of the resection defect after EMR: in a study conducted by Emmanuel *et al* [9], resection of an apparently normal mucosa at the lateral margin of the resection defect found that 19% of the specimens had histopathologic evidence of residual lesion, providing evidence that microscopic areas of adenomatous tissue can be left after resection, despite using standardized widefield EMR. Bahin *et al* [10] evaluated the use of a technique called extended EMR (X-EMR), which involves extending the resection to the apparently normal margins after EMR or piecemeal EMR, and compared that with standard wide-field EMR; however, they found no difference in recurrence. The authors hypothesized that residual tissue bridges probably remain uncaptured between areas of sequential snare capture. Recently, however, the ablation of the resection margins with soft tip snare coagulation (STSC) has shown impressive results in reducing AR after ER, resulting in a 4-fold reduction in AR rates at first surveillance colonoscopy [11]. Current ESGE guidelines [5] recommend thermal ablation of the margins using STSC to prevent AR after conventional EMR of LNPCPs. Regarding scar evaluation, results from a trial conducted by Kandel *et al* [12] on scar evaluation and the need of biopsies to detect AR found a high negative predictive value (NPV) and good diagnostic accuracy for virtual chromoendoscopy, with an especially high NPV of 100% using narrow band imaging

[a]Department of Medicine and Surgery, University of Bologna, Bologna, Italy (Tommaso Antenucci); [b]Gastroenterology and Endoscopy Unit, University Hospital Arcispedale Sant'Anna of Ferrara, Cona, Emilia-Romagna, Italy (Rosario Arena)

Conflict of Interest: None

Correspondence to: Tommaso Antenucci, University of Bologna, Department of Medicine and Surgery, Bologna, Emilia Romagna, IT, Resident Doctor in Gastroenterology and Digestive Endoscopy, Via Massarenti 9, Bologna (BO), 40138, Italy, email: tommaso.antenucci@studio.unibo.it

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(NBI) with near focus (NF) for the optical diagnosis of residual neoplasia when assessed with high confidence. These data strongly suggest that, in cases of high-confidence negative optical diagnosis based on NBI and NF, no biopsy is needed to confirm absence of recurrence during colorectal EMR follow up. In cases of low-confidence or high-confidence positive optical diagnosis, resection of any suspicious area would still be recommended. Current ESGE guidelines recommend careful evaluation of the scar with HD white-light imaging combined with virtual chromoendoscopy, instead of routine biopsy of the scar for the detection of AR [5]. The aim of this review is to provide an updated overview of the currently available endoscopic strategies for the management of locally recurrent colorectal adenomas.

Endoscopic strategies for the management of locally recurrent colorectal adenomas

Hot avulsion (HA)

HA is a modified version of the hot biopsy forceps avulsion of polyps. HA was first used by Veerapan *et al* [13], and involves the use of a hot biopsy forceps. Cut or coagulation current is applied to the non-lifting neoplastic tissue grasped with the forceps, with gentle mechanical traction applied if current alone is not able to completely resect the tissue; this process is then repeated until all visible neoplastic tissue is removed. In the study by Veerapan *et al*, 20 patients with non-lifting lesions were treated with HA, and only 1 delayed bleeding was reported as an adverse event. During follow up, the initial complete resection rate was 100%, with a 15% diminutive residual rate, easily treatable with repeat HA. Recent guidelines [5] recommend against the use of hot biopsy forceps for the resection of diminutive polyps, given its high rates of incomplete resection, inadequate tissue sampling and the unacceptably high risk of adverse events (deep thermal injury and delayed bleeding) in comparison with cold snare resection (CSR). However, it remains a valid solution for the removal of residual neoplasia that is not amenable to snare resection.

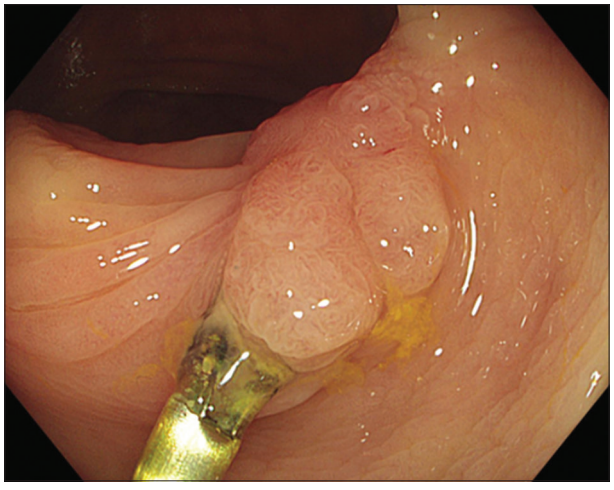

Figure 1 A recurrent adenoma of the ascending colon with a retained clip positioned in a previous endoscopic resection attempt

Cold-forceps avulsion with adjuvant soft tip coagulation (CAST)

CAST (Fig. 2A-D) is a novel technique described in 2018 by Tate *et al* [14]. This method has been used for the treatment of previously attempted non-lifting laterally spreading lesions (LSLs) and large non-lifting LSLs; it consists in isolating the lesion margins with standard snare excision and then performing cold-forceps avulsion of all visible non-lifting adenoma, with subsequent snare-tip soft coagulation of the exposed submucosa of the avulsion site and its margins. All the LSLs treated with CAST had a 100% success rate of removal of the non-lifting area (101/101 cases). Adverse events included 3 intraprocedural perforations, 12 deep mural injuries and 23 intraprocedural bleedings. After 2 follow-up procedures, 94/95 patients (98.9%) who underwent CAST had avoided surgery.

CSR

CSR (Fig. 3) is the most used and recommended technique for resecting polyps with dimensions <10 mm. Its advantages are the near zero risk of perforation and the low post-polypectomy bleeding rates. Recently, it gained popularity for treating large sessile serrated adenomas, using a technique called cold snare piecemeal polypectomy, which is currently available as an option for treating such lesions [5].

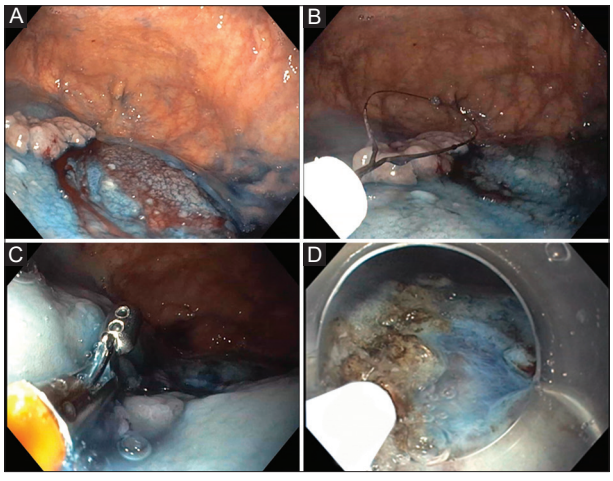

Figure 2 Cold-forceps avulsion with adjuvant soft tip coagulation CAST phases: (A) a recurrent cecal serrated adenoma with a double component (Paris IIa + IIb) showing a no lifting central portion. The procedure was executed with a gastroscope due to a very rigid sigmoid colon. (B) Snare resection of lifting portions. (C) Cold forceps avulsion of non-lifting central portions. (D) Soft tip snare coagulation of avulsed and resected margins

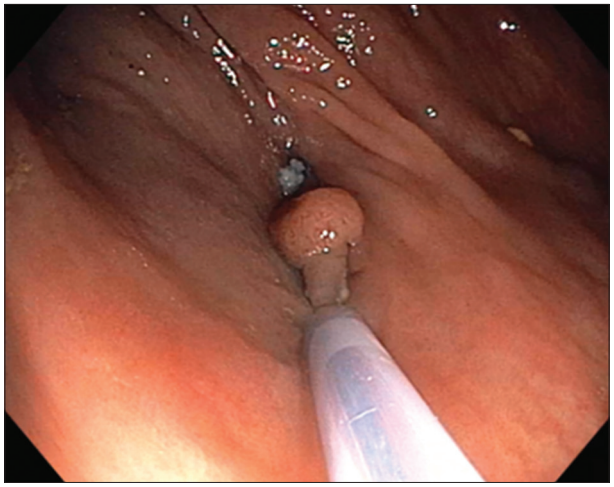

Figure 3 Cold snaring of a recurrent diminutive polyp of the transverse colon

A meta-analysis [15] that included 2592 polyps resected with CSR showed an excellent safety profile for this technique, with a pooled intraprocedural bleeding rate of 2.6% (95% confidence interval [CI] 1.5-4.5%, I^2=51%), a delayed bleeding rate of 1.5% (95%CI 0.8-2.7%, I^2=18%), with no reports of perforations or post-polypectomy syndromes, with estimated rates of 0.6% (95%CI 0.3-1.3%, I^2=0%) and 0.6% (95%CI 0.3-1.4%, I^2=0%), respectively. Polyp recurrence after CSR was 6.7% (95%CI 2.4-17.4%, I^2=94%). The recurrence rate was 12.3% (95%CI 3.4-35.7%, I^2=94%) for polyps ≥20 mm, 17.1 % (95%CI 4.6-46.7%, I^2=93%) for adenomas, and 5.7% (95%CI 3.2-9.9%, I^2=50%) for sessile serrated lesions. Data on recurrence when using this technique for larger lesions were confirmed in a comparison study by O'Sullivan *et al* [16], comparing CSR versus HSP for large >15 mm flat non-pedunculated polyps: the recurrence rate was significantly higher in the cold snare EMR group when compared to HSP (16/87, 18.4% vs. 1/90, 1.1%; relative risk [RR] 16.6, 95%CI 2.24-122; P<0.001), confirming the advice of the latest guidelines [5] on restricting this technique to lesions <10 mm. To our knowledge, there are no studies evaluating the use of this technique to treat AR.

EndoRotor®

The EndoRotor® device (Interscope Medical, Inc., Worcester, Massachusetts, United States) is an automated mechanical endoscopic device used for removing benign neoplastic or pre-neoplastic tissue in the gastrointestinal tract. This unique device has a fixed outer cannula with a hollow inner cannula that rotates; both cannulas have an opening that allows tissue suction and anchoring while the rotation cuts the trapped tissue. The removed tissue is constantly suctioned into a collection trap for subsequent pathological evaluation. A dedicated console controls the speed, which can be set to high (1750 rotations/min) or low (1000 rotations/min), and the suction, with options ranging between 50 and 200 mmHg of negative pressure. The device is operated by the endoscopist using a foot pedal. Its theoretical advantages are the absence of heat or ablation of the mucosa, leading to less scarring and a theoretical lower risk of perforation and bleeding; the possibility of using the device in a patient who has a pacemaker; the less probable muscular injury due to the fibroelastic properties of the mucosa while suctioned; and the capability of resecting large quantities of tissue. The main limitations of this device are a rather large catheter diameter, which requires a minimum working channel of 3.2 mm, meaning it cannot be used in slim endoscopes; the device stiffness, which limits the movement and flexibility of the scope, hindering its use in difficult locations or when retroflexion is needed; the quality of the collected tissue, which is similar to a biopsy specimen, and does not evaluate deep invasion margins; and its cost [17,18]. A prospective study by Kandiah *et al* [18], using this device for the treatment of 19 flat scarred polyps from previous attempts in the rectum and sigmoid colon, found that the overall cure rate (defined as the absence of adenomatous tissue on follow-up biopsies of the scar obtained 2 months after the first attempt) using EndoRotor® was 84%; 10 patients (52.6%) achieved cure after 1 attempt and 6 patients (31.5%) achieved cure after 2 attempts. Reported adverse events were 2 minor bleedings with no perforations, no post polypectomy syndrome and no delayed bleedings. Moreover, in a multicenter US study [19] that included 28 colorectal polyps, 25 of which had previously undergone treatment, EndoRotor® achieved complete resection in all patients. Seventeen (60.7%) patients underwent a follow-up endoscopy 2 months later and there was no recurrence in 15 (88.2%) patients. There were 4 intraprocedural bleedings and 2 delayed bleedings, all of which were endoscopically treated.

Underwater EMR (U-EMR)

U-EMR is a modified variant of EMR first described by Binmoeller *et al* [20] in 2012 for resecting large flat polyps. After reaching the target lesion, air is evacuated from the affected segment of lumen and completely replaced by water until complete filling is achieved. Under water immersion, the margins are diathermically marked with Argon plasma coagulation, and then resection can begin with ensnarement of the target lesion and subsequent application of cutting current. This technique was developed after endoluminal endoscopic ultrasound findings that, in a lumen filled with water, the *muscularis propria* does not change its position, and does not follow the changes of the mucosa and submucosa, so that lesions appear to float into the lumen, moving away from the *muscularis propria* and creating a "buoyancy effect" of the adenoma-bearing mucosa. Advantages of this technique include the magnification effect of water, which helps identify lesion margins and allows a more targeted application of the cutting current, thereby limiting mural injuries. Main drawbacks of this technique are the poor margin visualization capabilities in the setting of poor bowel preparation, and compromised visibility when there is contractility. Amato

et al [21] evaluated the feasibility of *en bloc* resection of colonic polyps using this technique, including 3 local ARs. All *en bloc* specimens had margins free of adenoma upon pathological examination, with a final *en bloc* resection rate of 76%. A meta-analysis conducted by Spadaccini *et al* [22], providing data on 508 resected lesions from 433 patients, found that the complete resection rate was 96.36%, with a rate of *en bloc* resection of 57.07%. The recurrence rate was 8.82% during a mean endoscopy surveillance period of 7.7 months. The postprocedural bleeding rate was 2.85%. Bleeding during the procedure was always mild, and was considered as part of the procedure in all series. The overall adverse event rate was 3.31%. No cases of perforation were reported.

Cap-assisted EMR (EMR-C)

EMR-C was first described by Inoue *et al* [23] in 1993. The tip of the endoscope is fitted with a transparent plastic cap, then the target lesion is lifted by injecting the submucosal layer with saline solution. Under full endoscopic suction, the lesion-involved mucosa is tightly packed inside the cap of the endoscope and then snared tightly and subsequently resected. Since 1993, many advances have been made: a study by Kashani *et al* [24]. evaluated the efficacy of EMR-C in resecting large non-pedunculated colorectal polyps. A total of 134 EMR-Cs were performed on 124 non-pedunculated colorectal lesions within a 55-month period, with a median follow up of 4.2 (1.6-46.8) months. Among the polyps with available follow up, the overall eradication rate was 91% (81/89) and the complication rate was 10.2%, with perforation reported in 3.9% of cases, intraprocedural bleeding in 3.9% and delayed bleeding in 2.4%. Although remaining of high concern, authors argued that the perforation rate could be lowered by increasing the fluid submucosal cushion and decreasing suction pressure before resecting. Another study by Van der Voort *et al* [25] evaluated the efficacy of EMR-C in 70 patients with non-lifting or fibrotic colorectal polyps, in which the most common cause of inadequate lift after submucosal injection was residual or recurrent adenoma. Complete macroscopic removal of polyp tissue was achieved in nearly all patients (68/70; 97.1%), with a 6-month recurrence rate of 6.7%, 14.3%, and 34.8% after EMR-C for target lesions of <10 mm (1/15), 10-19 mm (4/28) and >20 mm, respectively. The most common adverse event was deep mural injury, which occurred in 6 patients (8.8%), and delayed bleeding in another 6 patients (8.8%).

Full-thickness resection device (FTRD)

FTRD is a variant of the endoscopic full thickness resection (EFTR) technique, in which an over-the-scope dedicated device is fitted to the tip of a colonoscope. This device consists of a modified over-the-scope clip (OTSC) mounted on a transparent cap with a 23-mm depth and a 21-mm diameter. A 13-mm polypectomy snare is integrated in the cap, providing the cutting device needed for resection. The borders of the lesion are often marked with argon plasma coagulation or electrosurgical knife, then the lesion is retracted into the cap and, after deployment of the OTSC, resection can be achieved by applying cutting current through the integrated snare. This technique uses the "no hole" concept to prevent overt perforation and contamination of the peritoneal cavity. The most commonly reported adverse events include intra- and post-procedural bleeding, perforation and iatrogenic stenosis [26]. The over-the-scope mounted device is quite large and stiff, limiting maneuverability when navigating through severely rigid or diverticular colons, and making cecal intubation more challenging. In a German study [27], 70 patients, of whom 52 had recurrent adenoma, underwent colonoscopy for EFTR with FTRD. Resection was technically successful in 65 patients (97.0%). Histologically complete resection (R0) was achieved in 59/65 patients (90.8%). The R0 resection rate was lower for lesions >20 mm (86.5%) than for those ≤20 mm (92.9%). The total complication rate was 14.9%: there was 1 major complication (perforation of sigmoid colon), while other complications were mild. In another study, von Helden *et al* [28] conducted a retrospective case review of 30 consecutive EFTR procedures on small <20 mm, difficult to resect, recurrent or residual neoplastic lesions. EFTR was technically feasible in 28/30 (93.3%) of the cases, with an R0 resection in 24/30 (80%) and a median procedure time (marking to full thickness resection) of 34.5 min (11-120). One patient suffered from a delayed perforation the day after the procedure and needed emergency surgery (3,6%). Minor bleeding occurred in 3/28 patients (10.7%) and post-interventional fever in 1 patient (3.6%). The 30-day mortality rate was 0%.

ESD

ESD is an advanced resection technique. Originally pioneered in Japan for the treatment of early-stage gastric cancers, ESD has since gained global acceptance, and is now applied in various parts of the gastrointestinal tract, including the esophagus, stomach, colon and rectum. Unlike conventional EMR, which is limited to smaller lesions and often requires piecemeal removal, ESD enables precise and complete excision, regardless of lesion size, thereby reducing the risk of local recurrence and allowing for accurate pathological assessment. The ESD procedure involves several key steps: marking the lesion perimeter, submucosal injection to elevate the lesion, mucosal incision, and meticulous dissection of the submucosal layer beneath the lesion using specialized endoscopic knives. Although technically demanding and associated with longer procedure times and a higher risk of complications such as perforation and bleeding compared to EMR, ESD offers significant advantages in selected cases, particularly in preserving organ function and avoiding more invasive surgical interventions [29]. A study by Kuroki *et al* [30] evaluated the effectiveness

of ESD for residual or locally recurrent colorectal lesions following endoscopic therapy. A group of 34 recurrent and residual lesions treated with ESD were compared to a control group of 384 lesions treated in the same manner. ESD for residual/recurrent lesions achieved a high *en bloc* resection rate (100%) and curative resection rate (88.2%), despite the greater technical challenges, but with a significantly higher perforation rate (14.7% vs. 4.4%), probably due to severe fibrosis created by the previous ER attempts. Hurlstone *et al* [31] used ESD as a salvage technique to treat 30 cases of residual or local recurrent colorectal neoplasia, achieving R0 resection in 25 patients (83%) with an *en bloc* rate of 93%. No perforations were reported; immediate bleeding occurred in 16% of cases, all of which were endoscopically treated. AR is obviously associated with a greater presence of submucosal fibrosis, which can impact ESD outcomes, as demonstrated by Kim *et al* [32]: perforation was found more often in F2 fibrosis, and the complete resection rate in the F2 group was 63.0%, which was significantly lower than that in the F0 and F1 groups combined (97.3%). Another recent Italian multicenter prospective study [33] of the use of ESD for the management of fibrotic non-lifting large colon polyps included a cohort of 178 lesions, 126 of which were recurrences: the overall recurrence rate after ESD was 3.3%, with a total of 6 recurrences observed at the first surveillance colonoscopy (median 190 days) among 167 patients, after excluding those referred for surgery, confirming the high success rate of this technique in treating complex and fibrotic lesions.

Discussion

ER of colorectal adenomas has revolutionized the management of pre-neoplastic lesions, significantly reducing the progression to CRC [4]. However, the risk of AR after ER remains a notable challenge, with factors such as lesion size, high-grade dysplasia and piecemeal resection being key contributors to recurrence [6-8]. To address these recurrences, commonly available and advanced endoscopic techniques have emerged, offering promising outcomes but presenting specific limitations and challenges. The choice of technique is influenced by lesion characteristics, operator preference, center expertise and patient factors. In our experience, the safest and easiest appliable techniques are CAST and CSR. These 2 techniques are cheap, widely available, do not require advanced training or dedicated devices, and can usually treat most of the recurrences encountered. Small recurrences are excellently managed with these 2 methods. Possible limitations of the cold snare technique may include the limited capacity to grasp tissue on a fibrotic scar and achieving a radical resection, with a histological specimen limited to the mucosa or initial submucosa. As CAST [14] uses diathermy, it may carry a greater risk of deep mural injury, and it can be time-consuming in large recurrences. As it is expensive and not widely available, we think that EndoRotor® should be reserved for selected cases, such as large benign flat lesions with no sign of deep submucosal invasion. Among the advanced techniques discussed, ESD and U-EMR stand out for their ability to achieve high rates of *en bloc* resection. ESD, despite being technically demanding and associated with a higher risk of perforation, particularly in high submucosal fibrosis lesions such as recurrences [32], has shown impressive *en bloc* and curative resection rates [30,31]. It can also effectively resect large lesions with uncommon shapes. Conversely, U-EMR offers a less invasive alternative, with advantages such as reduced mural injuries, though visibility issues can limit its application if bowel preparation is suboptimal. This technique can grasp large lesions, aided by the buoyancy effect generated by water, with limited perforation rates. EMR-C excels in addressing fibrotic and non-lifting polyps, because of the use of suction and a plastic cap. FTRD provides a "no hole" approach, particularly advantageous in lesions with severe fibrosis, but it has some limitations, such as difficulty in reaching lesions located in the proximal colon, or in advancing through a diverticular colon or rigid segment, due to the large device mounted on the tip of the scope. This requires great expertise in navigating the device in the colon to avoid injury during the insertion phase. Large or laterally spreading lesions may not be fully included in the plastic cap, impeding complete resection.

We usually divide these techniques into *ablative* and *resective* techniques. Ablative techniques, such as HA, CAST and EndoRotor®, do not produce a multilayer histopathological specimen if the avulsed parts are sent to analysis, with CAST being limited to the most superficial mucosal layer. Submucosal invasion evaluation is thus not available: this should be considered when scar interrogation with NBI suggests deeper invasion. Resective techniques, such as U-EMR, EMR-C, FTRD and ESD, make this analysis possible, but they obviously bear a higher risk of perforation and deep mural injury. FTRD is the only technique that produces a "full thickness" specimen, making pathological analysis possible from the mucosa to the serosa. Despite advances, challenges like recurrence after primary resection, technical difficulties and procedure-associated risks remain. A tailored approach, combining lesion-specific characteristics and endoscopist expertise, is critical for optimizing outcomes. Furthermore, robust follow-up protocols and improvements in imaging and detection techniques can enhance the early identification and management of recurrences. This is the only available review discussing endoscopic strategies for the management of recurrent colorectal lesions, giving the endoscopist the opportunity to assess and choose which technique is the most suitable for a specific case and highlighting the strengths and downsides for each strategy. A summary of the available techniques is available in Table 1.

In conclusion, while endoscopic techniques for treating recurrent adenomas have evolved significantly, there remains a need for continued innovation and standardized guidelines to balance efficacy with safety. Future research should focus on refining these strategies, incorporating emerging technologies, and exploring synergistic approaches to further reduce recurrence rates and improve patient outcomes.

Table 1 Summary of the available techniques, with advantages and disadvantages, most frequent adverse events and R0 resection rates reported for recurrence

Technique	Type	Advantages	Weaknesses	Most frequent adverse events	Histological R0 reported rates for recurrence treatment
Hot avulsion	Ablative	Easy to apply	Device not easily found because hot biopsy forceps for polyps has been largely abandoned	Deep mural injury Perforation Bleeding	R0 data not available as it is an ablative technique
CAST	Ablative	Easy to apply Cheap	Time consuming in large lesions	Deep mural injury Perforation	R0 data not available as it is an ablative technique
EndoRotor®	Ablative	Resection of large mucosal areas Doesn't use diathermy	Expensive Not readily available in all centers Limits scope maneuverability	Bleeding	R0 data not available as it is an ablative technique
Underwater EMR	Resective	Easy to apply Cheap	Requires confidence with underwater techniques Poor visualization if sub-optimal bowel preparation	Deep mural injury Perforation	No specific study on R0 rates in treating recurrence
Cap-assisted EMR	Resective	Easy to apply Cheap	Requires experience in using a distal cap Cap accommodates only small lesions	Deep mural injury Perforation	Histological R0 is not available in current studies Van Der Voort *et al.* report 97.1%[25] complete macroscopic resection rate
FTRD	Resective	Enables full thickness resection and histological analysis Relatively fast once lesion is reached Great grasping capabilities	Expensive Requires great experience to navigate the scope with the device attached Limited reach in proximal colon or severely rigid or diverticular colons Large lesions or laterally spreading lesions may not be fully included in the plastic cap	Perforation Bleeding Clipping of nearby organs Iatrogenic stenosis of involved tract Clip misdeployment	Von Helden *et al.* 80%[28] Albrecht *et al.* 90.8% [27]
ESD	Resective	Appliable to large lesions with unconventional shapes Good histological staging capabilities	Expensive Time consuming Requires great experience, even if the operator commonly performs ESD, due to high difficulty in dissecting fibrotic areas	Deep mural injury High risk of perforation Bleeding	Kuroki *et al.* 82%[30] Hurlstone *et al.* 83%[31]
Cold snare	Resective	Cheap Widely available	Low capability of grasping tissue on a fibrotic scar	Very low rates of post polypectomy bleeding, Near zero risk of perforation	No specific study on R0 rates in treating recurrence

CAST, cold-forceps avulsion with adjuvant soft tip coagulation; EMR, endoscopic mucosal resection; FTRD, full-thickness resection device; ESD, endoscopic submucosal dissection

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