Endoscopic resection of large colorectal polyps: a narrative review of the literature and best practices for management

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Objective and Background: It is well established that early detection of precancerous lesions and their prompt removal can effectively reduce the incidence of colorectal cancer (CRC). Polyps of 10 mm or larger, although less prevalent, have higher risk of advanced pathology and require careful examination by the endoscopist to determine the most efficient resection method to ensure complete resection with the lowest recurrence and complication rates. We aim to conduct a narrative review of the current literature on the latest advances in endoscopic resection techniques for management of large colorectal polyps and to provide evidence based-guidance to improve patient care and to reduce unnecessary surgeries.

Methods: We conducted a comprehensive literature review of pertinent English-language articles using different electronic databases (PubMed, Embase and Cochrane) from the database's inception until August 1st, 2021, and examined the latest guidelines from major gastroenterology societies to compile this narrative review.

Key Content and Findings: Pedunculated polyps ≥ 10 mm are best removed by hot snare polypectomy (HSP) with ligation of the stalk if its thickness ≥ 5 mm. Non-pedunculated polyps ≥ 10 mm with lower likelihood for submucosal invasion can be effectively removed by conventional inject and cut endoscopic mucosal resection (EMR), while those $\geq 20-30$ mm with higher likelihood for superficial submucosal invasions could be considered for endoscopic submucosal dissection (ESD) in experienced centers. Since conventional EMR and ESD have higher complication and recurrence rates, newer resection techniques are being investigated, including cold snare EMR (CS-EMR) that potentially has less bleeding or perforation risks, underwater EMR (UEMR) with promising higher *en-bloc* resection rate for larger polyps, and full-thickness resection using a special device for non-lifting lesions or those in difficult locations that were previously thought unresectable endoscopically.

Conclusions: Future prospective studies are required to better characterize eligible lesions for individual techniques to improve patient care and reduce recurrence rates and referral to surgery for management.

Keywords: Colorectal cancer (CRC); colonoscopy; polypectomy

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Introduction

Colorectal cancer (CRC) is the 2nd most common cancer in the United States contributing to a leading cause of morbidity and mortality. CRC will be responsible for an estimated 52,980 deaths in year 2021, despite improvement in screening modalities and early treatment (1,2). It starts as a glandular growth in the epithelial cells of the colorectal mucosa in 90% of the cases (3) forming detectable polyps that can be removed before they turn into cancer. Colonoscopy currently offers a screening and therapeutic test of choice that is less invasive than surgery and has shown to reduce population prevalence of CRC. Although different appearance-based classifications such as Paris, Kudo, NBI international colorectal endoscopic (NICE) and Japanese NBI expert team (JNET) have been developed to predict deep submucosal invasion of $\geq 1,000 \,\mu\text{m}$, a marker of higher risk of malignancy, the size of the neoplastic lesions remains an independent and important predictor of malignancy.

In this article, we review endoscopic recognition and management of large colorectal polyps. We also review the latest literature on conventional and novel endoscopic resection methods, the risk of cancer recurrence after endoscopic resection and the role of surgery in such lesions. Finally, we propose an easy-to-follow approach to large polyps management.

We present the following article in accordance with the Narrative Review reporting checklist (available at https://dmr.amegroups.com/article/view/10.21037/dmr-21-61/rc).

Methods

A literature search was conducted using electronic databases (PubMed, Embase and Cochrane) to identify Englishlanguage articles published from the database's inception until August 1st, 2021. Keywords included "colorectal cancer", "colon cancer", "colon polyps", "large polyps", "polyp resection", "management" and "polypectomy". Abstracts were individually screened and selected by both authors (AGT, MD). We further narrowed the screening by examining available randomized controlled trials, multicenter studies, comparative studies, clinical trials, and observational studies, in addition to meta-analyses, systematic reviews, evidence-based practice recommendations by societies and published guidelines (*Table 1*).

Discussion

Large colorectal polyps and risk of malignancy

Any colorectal lesion larger than 10 mm is considered large (4). Depending on its morphology, it could be pedunculated or sessile. Polyps larger than 10-20 mm in size and expanding more horizontally than vertically are described as laterally spreading tumors (LST). Lesions >10 mm in size are common and have gained special interest and attention due to their higher potential for harboring malignancy, up to 2.41% for lesions 10-20 mm and 19.35% for lesions >20 mm (5-7). Reinhart et al. assessed 17,771 patients with colorectal polyps and reported a risk of high-grade dysplasia (HGD) of 8.82% in polyps >10 mm, compared to 0.87% in smaller polyps $\leq 10 \text{ mm}$ (8). The risk of residual or recurrent adenoma (RRA) on follow up at the site of prior initial resection also increases as the lesion size increases, as reported by a pooled analysis of 8 prospective studies conducted by Martínez et al. which found that advanced adenoma recurred in 15.9% [95% confidence interval (CI): 14.5-17.4%] of lesions 10-20 mm and 19.3% (95% CI: 16.4–22.3%) in lesions ≥20 mm size. The risk for cancer on follow-up was 1.2% (95% CI: 0.4-2.0%) in lesions \geq 20 mm (9). Endoscopic resection of large lesions, instead of surgery, has become the standard of care in the last few years, though interestingly and for unclear reasons, the rate of surgical resection of benign lesions had doubled between 2000 and 2014 in the US (10) suggestive of unnecessary surgeries and additional morbidity among this group. Surgery adds morbidity related to colectomy and subsequent complications. On the other hand, endoscopic resection offers curative removal with minimal risk of recurrence if done at early stage.

Due to their size, larger polyps, especially LSTs, are at risk for RRA. Incomplete resection of lesions contributes up to 19% of interval CRC after recent colonoscopy, hence endoscopists should aim to achieve negative histologic margins at polypectomy (R0) (11). *En-bloc* resection is preferred whenever possible, usually for lesions <20 mm, due to lower complications and risk of RRA (7). Nonetheless, large, nonpedunculated lesions are more commonly to be resected in a piecemeal fashion, which has up to 5.5 times higher risk of RRA compared to *en-bloc* resection (12). As such, the European Society of Gastrointestinal Endoscopy (ESGE) recommends the least number of pieces when performing piecemeal resection (13).

Digestive Medicine Research, 2021

Table 1 The search strategy summary

Items	Specification	
Date of search (specified to date, month and year)	August 15, 2021	
Databases and other sources searched	PubMed, Embase, Cochrane	
Search terms used (including MeSH and free text search terms and filters)	Colorectal cancer, colon cancer, colon polyps, large polyps, polyp resection, management, polypectomy	
Timeframe	Database inception to August 1, 2021	
Inclusion and exclusion criteria (study type, language restrictions etc.)	English-language only articles. Single case reports were excluded	
Selection process (who conducted the selection, whether it was conducted independently, how consensus was obtained, etc.)	Selection was conducted by both authors (AGT, MD)	
Any additional considerations, if applicable	Not applicable	

Role of endoscopic resection

Endoscopic resection is currently considered the standard method of management for precancerous polyps including those with intramucosal cancer. This is also the test of diagnosis, staging and potential curative removal before determining the next step for majority of polyps. While the role of colonoscopic resection continues to expand, it is generally limited to lesions with less than 1,000 µm of submucosal invasion (13,14). The success rate of endoscopic resection can be predicted by using the self-explanatory size, morphology, site, and access score (SMSA) developed by Sidhu *et al.* (15). The score assigns lesions into four main categories (SMSA 1 to 4), with the lowest procedural success rate of 93% for SMSA 4 (15).

The United States Multi-Society Task Force (USMSTF) comprised of gastroenterologists from three different American societies, as well as the ESGE provide up-todate guidelines on colorectal lesions management in the Western world. While Eastern endoscopists primarily find such guidance provided by the Japan Gastroenterological Endoscopy Society (JGES) guidelines (13,14,16).

Conventional endoscopic resection methods

Polyp morphology, size, location, and features of submucosal invasion among other characteristics would determine the preferred resection method. Conventional endoscopic resection methods for large polyps include use of snare with thermal energy (cautery) for resection with or without submucosal injection. Pedunculated lesions measuring ≥ 10 mm should be removed by hot snare polypectomy (HSP) through the middle to lower stalk with ligation of the stalk if the head size ≥ 20 mm or stalk thickness ≥ 5 mm (13,14). HSP has a good complete resection rate of >80% with low complications rate (17,18).

Non-pedunculated lesions of 10–19 mm in size have also been traditionally removed by HSP with submucosal injection recommended to reduce thermal injury (13). Alternatively, cold snare polypectomy (CSP) with or without submucosal injection has shown complete resection rate of 99.3% (95% CI: 98.6–100%) with residual rate of any histology of 4.1% (95% CI: 0.2–8.4%) (19). This is reflected in the USMSTF recommendations of either cold or HSP for such lesions (14). When it comes to sessile serrated polyps (SSP) of this size, conventional or CSP with endoscopic mucosal resection (EMR) appears to be effective with low RRA as shown by a meta-analysis by Thoguluva Chandrasekar *et al.* (20).

Historically, larger polyps including LSTs measuring \geq 20 mm used to require surgical resection, until recent emergence and improvements of endoscopic resection techniques over the past few decades. These lesions can be effectively treated endoscopically in up to 90% of the cases (21). EMR is now the preferred endoscopic method as it is widely accessible, relatively safe to perform and has high success rate achieving complete resection close to 90% (21-23). It involves lifting the polyp by injecting

Table 2 Data from available literature on various methods of large colorectal polyp resection with data on efficacy, adverse events and recurrence rates

Polypectomy method	Lesion morphology and size	Efficacy (R0 or en-bloc)	Adverse events	Recurrence
HSP	Non-pedunculated lesions 10–19 mm and pedunculated lesions ≥10 mm	81% (17)	1–3.7% overall (17,18)	48% of SSL (30)
CSP	Non-pedunculated lesions ≤19 mm	82–89% (17)	0.2-6.6% overall (17,18)	Up to 9.7% (31)
Conventional EMR	Non-pedunculated lesions and LSTs ≥20 mm, SSL 10–19 mm	80–90% (20,21,26)	1.2–1.5% perforation (21, 26), 6.9–9.6% bleeding (21,26)	4.3% in serrated lesions (20), 13% (21,26,27)
CS-EMR	Non-pedunculated lesions and LSTs ≥20 mm	-	-	5.5% (32)
UEMR	Non-pedunculated lesions and LSTs ≥20 mm	57% (33)	3.3% overall, 2.8% bleeding (33)	8.8% (33)
ESD	Non-pedunculated lesions and LSTs ≥20 mm	93.6% in LST (26)	6% perforation (26), 2.8% bleeding (26)	1.1% (26)
Hybrid ESD	Non-pedunculated lesions and LSTs ≥20 mm	81.6% (34)	4.6% perforation, 4.3% bleeding (34)	4.5% (34)
eFTR (FTRD)	Any lesion morphology or size not amenable for resection by other methods	80% (35)	12% overall (35)	13% (35)

HSP, hot snare polypectomy; SSL, sessile serrated lesion; CSP, cold snare polypectomy; EMR, endoscopic mucosal resection; LST, laterally spreading tumor; CS-EMR, cold snare endoscopic mucosal resection; UEMR, underwater endoscopic mucosal resection; ESD, endoscopic submucosal dissection; eFTR, endoscopic full-thickness resection; FTRD, full-thickness resection device; R0, negative histologic margins at polypectomy.

a solution, usually saline, into the submucosal space underneath the lesion of interest to separate it from the muscular layer and to create a cushion before tissue resection to minimize the risk of perforation. Though few drawbacks have been described with EMR, that include clinically significant post-EMR bleeding (CSPEB) in up to 10% of the cases and deep mural injury (DMI) leading to perforation in 1.5% (14,21,24-26). Another drawback is the further enlargement of the lesion after the submucosal injection, necessitating more frequent piecemeal resection which in turn could increase the risk of incomplete resection. Conventional EMR carries a recurrence rate of approximately 20% when piecemeal resection was performed and 3% when en-bloc resection was performed (27-29). Hence, the USMSTF recommends surveillance colonoscopy post-EMR resection at 6 months, 18 months, and 4.5 years, and the ESGE offers similar recommendations (13,14). Table 2 reviews the recurrence and complication rates of conventional and novel methods.

For larger polyps, endoscopic submucosal dissection

(ESD) offers a valuable alternative resection method that can achieve *en-bloc* resection more consistently, especially in lesions with high suspicion of superficial (<1,000 μ m) submucosal invasion with virtually no size limit (14,36). Compared to EMR, ESD has higher curative resection rate (93% *vs.* 84%) and markedly less recurrence rate (1.1% *vs.* 13%) (21,26). One major downside of ESD is the high perforation rate of 6%, therefore it is usually confined to experienced centers (26).

Novel endoscopic resection methods

Novel endoscopic techniques have been suggested and studied in hope to further decrease the risk of RRA and reduce complications that are attributed to conventional methods. Such novelties are simple, such as the simple thermal ablation of post-EMR margins using snare tip soft coagulation (STSC) which could potentially reduce the recurrence rate down to 5% compared with 21% in the control group who did not receive any additional treatment post-EMR as reported by Klein *et al.* (37). Based on this data, STSC is currently suggested to reduce postpolypectomy recurrence mainly for LSTs >20 mm in size.

Another novelty is using cold snare EMR (CS-EMR) instead of the traditional hot snare as it was recently found to be equally effective and perhaps with less CSPEB and DMI (32). Another new approach to remove large SSP, is by forego EMR and perform piecemeal cold snare polypectomy (p-CSP). In a comparative study, no complications were identified in 121 patients in the p-CSP group, compared to 45 total events in 353 patients in the EMR group (38).

Underwater EMR (UEMR) was first described by Binmoeller *et al.* in 2012, that aims at achieving higher success rate in *en-bloc* resection of large LSTs, by eliminating submucosal lifting prior to resection and immersing the lesion with water instead of gas insufflation (39). Binmoeller *et al.* reported complete *en-bloc* resection of 29 out of 50 LSTs (55%) with R0 confirmed histologically in 79% of those 29 LSTs (40). UEMR superiority to conventional EMR, especially for flat and sessile lesions \geq 20 mm, was suggested by recent meta-analyses showing improved *en-bloc* resection rates with odds ratio (OR) up to 2, and notably lower RRA with OR 0.3 (41-43). Additionally, UEMR showed promising results when attempted on lesions at difficult locations such as the appendiceal orifice (44).

The underwater technique can be adopted in other polypectomy methods to be used for lesions of different sizes and morphologies including pedunculated polyps. This technique has shown to be more efficient by decreasing the procedural time with significantly less immediate bleeding in comparison to traditional gas insufflation polypectomy as reported by Cadoni *et al.* (45).

It is common in practice to encounter colorectal lesions that are not amenable to any of the endoscopic resection methods described above, such as non-lifting lesions and those arising from a difficult location like the appendiceal orifice. However, a novel device was recently developed to achieve endoscopic full-thickness resection (eFTR) [eFTR via FTR device (FTRD)] instead of invasive surgery. This technique was recently evaluated in 65 centers across Germany in a real-world clinical setting. R0 resection was achieved in 80% of 1,178 eFTR procedures, with RRA rate of 13.5% in 683 follow-ups (35). Those excellent findings were consistent in both lesions measuring <20 mm as well as those measuring \geq 20 mm (35). There is also growing interest in using eFTR for T1 CRC as both a therapeutic as well as a diagnostic option by providing full-thickness specimen allowing high quality histological assessment (46). Lesions 25–30 mm with adenoma recurrence or suspected submucosal invasion are candidates but the practical applications are much broader for eFTR which are in evolution including need for R0 resection, fibrotic lesions and previously resected benign lesions. Hybrid EMR-eFTR (or ESD) are also an option for residual fibrotic lesion or suspected area of submucosal invasion where rest of the lesion (even larger than 3 cm) can be removed by conventional technique followed by eFTR/ESD of the residual area that needs to be removed *en-bloc* for precise assessment.

Role of surgical resection

The role of surgical resection is now reserved to colorectal lesions with signs suggestive of deep submucosal invasion with probable lymphatic spread (13,14). Lesions where prior endoscopic resections have been attempted with persistent concern for submucosal invasion and lesions located in difficult anatomical locations (i.e., lesions extending inside appendicular orifice, terminal ileum) are also referred to surgery. The role of endoscopy continues to expand in management of such lesions and with advent of FTRD and ESD, now majority of benign lesions are removed by endoscopic means. Referral to advanced endoscopist or expert in managing colorectal lesions should be pursued prior to sending them for surgery. We are proposing a step-by-step approach for management of large colorectal polyps while incorporating current recommendations (Figure 1).

Summary

In conclusion, large benign colorectal lesions are amenable to endoscopic resection in majority of cases. The determination of lesion size, morphology, features of submucosal invasion and competence in resection strategy that can achieve effective complete resection with least adverse events are essential. In present time, no benign colorectal polyps should undergo surgery for removal unless absolutely needed and such cases should be reviewed with an advance endoscopist prior to surgery. The field is evolving, and more methods of endoscopic resection will be available offering personalized precision medicine for individual lesions with hope for better outcomes for all patients.

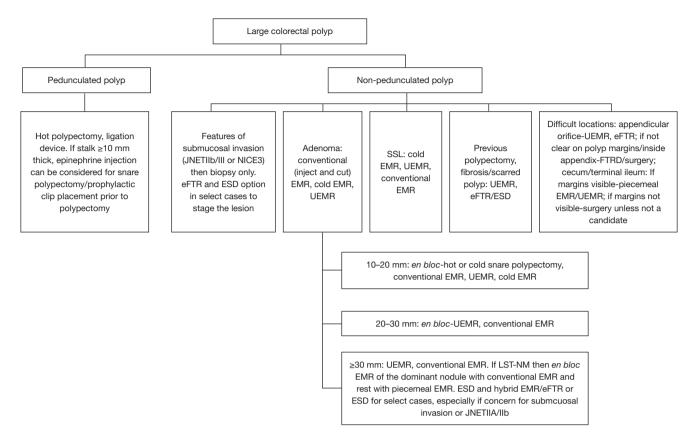


Figure 1 Proposed step-by-step management algorithm. JNET, Japanese NBI expert team classification; NICE, NBI international colorectal endoscopic classification; EMR, endoscopic mucosal resection; UEMR, underwater endoscopic mucosal resection; SSL, sessile serrated lesion; eFTR, endoscopic full-thickness resection; ESD, endoscopic submucosal dissection; FTRD, full-thickness resection device; LST-NM, laterally spreading tumor nodular mixed.

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Footnote

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