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EDITORIAL

Large non-pedunculated colorectal polyp management: The elephant in the room

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Abstract

Minimally invasive innovations have transformed coloproctology. Specific to colorectal cancer (CRC), there has been a shift towards less invasive surgical techniques and use of endoscopic resection as an alternative for low risk T1 CRC. The role of endoscopic resection is however much more extensive: It is now considered the first line management strategy for most large (≥ 20 mm) non-pedunculated colorectal polyps, the majority of which are benign. This is due to the well-established efficacy, safety, and cost-effectiveness of endoscopic techniques compared to surgery. Multiple endoscopic modalities now exist with distinct risk-benefit profiles and their outcomes are further improved by site-specific technical modifications, auxiliary techniques, and adverse event mitigation strategies. Endoscopic capacity continues to evolve with emerging endoscopic techniques and expanding applications, particularly in the confines of a multi-disciplinary setting.

Key Words: Cancer; Colonoscopy; Endoscopy; Polyp; Endoscopic mucosal resection; Endoscopic submucosal dissection

Core Tip: There is a movement towards minimally invasive management of colorectal disease, including the use of less invasive surgical techniques for colorectal cancer. Similarly, a paradigm shift in endoscopic resection has led to the development of a gamut of techniques, which are now first-line management strategies for most large (≥ 20 mm) non-pedunculated colorectal polyps (LNPCPs) - the majority of which are benign. This is due to their proven efficacy, safety and cost-effectiveness compared to surgery. With increasing detection of LNPCPs in universal screening programs, further adoption of an endoscopic approach in the era of minimally invasive resection techniques is anticipated.

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INTRODUCTION

The shift towards minimally invasive treatment strategies has been pervasive in gastroenterology and general surgery, including the practice of coloproctology. The introduction of laparoscopic surgery to the management of colorectal disease led to a reduction in morbidity, mortality, duration of hospitalization and rate of ostomy formation, while maintaining long term efficacy compared to open surgery[1,2]. Robot-assisted surgery has also demonstrated superior safety and cost-effectiveness, despite being more resource-intensive[3]. More recently, transanal endoscopic surgery (TES) permits local excision of early stage rectal cancer while preserving the anal sphincter and autonomic nerves, with an advantageous safety profile[4]. In contrast, radical resection, particularly in the rectum, emphasizes the potential risk of surgery on morbidity, mortality, and quality of life. Efforts to avoid these risks have driven advances in the medical management of inflammatory bowel disease and neoadjuvant chemoradiotherapy for rectal cancer, as discussed by Emile and Ragheb[5].

MINIMALLY INVASIVE ENDOSCOPIC RESECTION FOR LARGE POLYPS

As an extension of minimally invasive treatment strategies, Emile and Ragheb[5] introduce the use of endoscopic resection techniques, specifically endoscopic submucosal dissection (ESD) and endoscopic full thickness resection (EFTR) for low-risk T1 colorectal cancer (CRC) as an alternative to surgery[5]. However, malignant lesions represent only a fraction of large (≥ 20 mm) non-pedunculated colorectal polyps (LNPCPs), with submucosal invasion identified in up to 16% of LNPCPs selected for *en-bloc* endoscopic resection[6]. Rather, LNPCP considered in aggregate are commonly encountered in approximately 1 in 13 patients with fecal immunochemistry test positivity[7]. LNPCPs were historically managed by surgery, which can be associated with 25.3% morbidity and 0.8% in-hospital mortality[8]. Despite this, the rate of surgery for benign colorectal polyps continues to rise in the United States[9].

Recently, endoscopic resection has become the first-line management strategy for most LNPCP due to its comparable efficacy but superior safety and cost-effectiveness compared to surgery[10]. In a meta-analysis of 50 studies including 6779 large polyps (benign and malignant) undergoing endoscopic resection, 96.3% of procedures were successful and 92% avoided surgery. Surgery due to adverse events occurred in 1% and mortality-related to endoscopic resection was 0.08%[11]. Compared to minimally invasive laparoscopic surgery, endoscopic resection for complex colorectal polyps was more cost effective and yielded greater quality-adjusted life-years[12].

Amongst techniques, endoscopic mucosal resection (EMR) is preferred for most LNPCPs[10]. High-quality EMR is now well established[13]. Firstly, submucosal injection of colloid lifts the LNPCP to facilitate capture of polypoid tissue into a snare. An electrocautery current is then applied to transect the tissue. Following this, careful inspection of the defect is carried out for further polypoid tissue or signs of injury. Depending on size, further resections are systematically completed until all polypoid tissue and a margin of normal mucosa has been removed. Following successful EMR, a prospective study of 1000 consecutive LNPCP reported 98.1% were adenoma-free and avoided surgery at 16 months[14]. Due to its efficiency and safety, EMR has demonstrated significant cost savings and reduction of 2.81 nights of admission per patient compared to surgery[15].

The safety of EMR is owed to advancements in adverse event mitigation. The most common adverse event following EMR is clinically significant bleeding, with higher risk in larger lesions and proximal location[16]. A recent systematic review and meta-analysis including 4 randomized controlled trials found that prophylactic clip closure in the proximal colon significantly reduced bleeding from 9.0% to 3.5%[17]. Perforation, the most feared complication of endoscopic resection, can be mitigated by standardized evaluation of deep mural injury (DMI) and timely prophylactic closure. In a prospective cohort of 3717 LNPCP, significant DMI occurred in 2.7% of cases, of which 97.0% were successfully clipped without further sequelae[18]. Post-EMR recurrence is mitigated by thermal ablation of the post-EMR margin, supported by evidence from a randomized controlled trial demonstrating recurrence rates of 5.2% and 21.0% in the treatment and control groups, respectively[19]. Finally, if residual or recurrent adenoma is found on subsequent surveillance, it can generally be endoscopically treated with less than 5% of recurrences requiring surgery[20].

Further, site-specific modifications and auxiliary techniques improve technical success in challenging LNPCP[21-23]. Non-lifting lesions prone to incomplete resection can be treated with cold-forceps avulsion with adjuvant snare-tip soft coagulation, which has been shown to reduce rates of surgery to mirror more straightforward lifting lesions[23]. Thus, endoscopic resection is recommended even for complex LNPCP that have been historically designated for surgery. Previously attempted, circumferential (≥ 90% of the lumen), peri-appendiceal, ileocecal valve, and anorectal junction LNPCP can be endoscopically removed with 90%-95% success in expert hands[21-25].

Cold snare resection (CSR) is gaining recognition as an important resection technique, particularly for serrated lesions. Similar to EMR, CSR is a systematically applied snare technique to remove all polypoid tissue but utilizes mechanical transection rather than electrocautery, thus limiting thermal injury. While it was initially presumed to trade efficacy for safety, this has not borne out in the evidence. Particularly, serrated LNPCP appear to be uniquely amenable to CSR due to their low profile and rare frequency of submucosal fibrosis. In a comparative study of large sessile serrated lesions treated with CSR or EMR, the rates of recurrence, bleeding, and DMI were 4.3%, 0.0%, and 0.0% for CSR and 4.6%, 5.1%, and 3.4% for EMR[26].

For malignant LNPCP, *en-bloc* endoscopic resection can achieve oncologic cure as illustrated by Emile and Ragheb's discussion of ESD and EFTR[5]. Specifically, low risk T1 CRC is defined by the absence of lymphovascular invasion, poor differentiation, high-grade tumor budding and deep submucosal invasion (≥ 1000 μm), in the setting of *en-bloc* resection with negative histologic margins (R0); the presence of any unfavorable characteristic designates the lesion as high risk[27-29]. Lesions without a high-risk feature have a low risk of lymph node metastasis, with a meta-analysis of 71 studies of 5167 patients demonstrating pooled incidence of local and distant recurrence for low risk T1 CRC of 0.7%, compared to 7.0% if any high risk criteria were found[30]. Thus, endoscopically resected low risk T1 CRC is considered "curative" while high risk T1 CRC requires consideration for completion oncologic surgery.

For T1 CRC, multiple treatment modalities are available. A meta-analysis including 19979 patients with T1 CRC found that patients undergoing primary endoscopic resection and surgery had similar disease-free survival of 94.8% and 96.5%, respectively but lower rate of procedure-related adverse events at 2.3% and 10.9%, respectively[31]. Given the limited ability of EMR to achieve *en-bloc* resection for lesions greater than 20 mm, ESD is preferred for LNPCP with endoscopic signs of superficial submucosal invasive cancer (SMIC)[28,32-34]. ESD uses an electrosurgical knife to dissect in the submucosal plane beneath the lesion, thus allowing for *en-bloc* resection regardless of size. However, ESD has limited success in cases of submucosal fibrosis and deep invasion, leading to development of EFTR. While multiple techniques exist, EFTR is the colorectum generally uses an over-the-scope clip (OTSC) and snare resection. Using the full-thickness resection device (Ovesco Endoscopy; Tübingen, Germany), the lesion is pulled into a cap, facilitating OTSC closure of the duplicated colonic wall, and finally a pre-loaded snare completes the resection above the clip[35]. Alternatively, transanal endoscopic surgery (TES), encompassing both transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS), utilizes surgical instruments to enable full thickness excision. Compared to ESD, TEM has similar rate of curative resection and adverse events but can be more time and resource intensive[36].

Emerging endoscopic techniques for T1 CRC include endoscopic intermuscular dissection (EID) in the rectum and cooperative endoscopic laparoscopic surgery (CELS) in the colon. EID uses an electrocautery knife to dissect between the circular and longitudinal layers of the muscularis propria in the rectum, achieving deeper margins while preserving the rectal wall[37]. An example of CELS is colonoscopy-assisted laparoscopic wedge resection, whereby laparoscopic resection is guided by direct endoscopic visualization to facilitate more precise full-thickness resection[38]. Newer techniques can be expected in the near future.

The number of endoscopic techniques corresponds to the heterogeneity in LNPCPs, highlighting the role of optical diagnosis to determine the most appropriate modality. Optical evaluation uses a combination of size, location, surface pattern, morphology, and gross morphologic features to predict histopathology, and SMIC presence and depth. In the absence of optical features, covert or invisible SMIC may still exist in some LNPCP; this risk can be defined by location, morphology, and granularity[39]. Accurate prediction of SMIC has been shown to facilitate more deliberate use of *en-bloc* resection techniques, such as ESD, which are curative but more resource intensive. Unsurprisingly, selective use of EMR and ESD is the most cost-effective strategy to balance procedural cost and additional completion surgeries[40]. In the rectum where malignancy risk is substantial, use of a selective resection algorithm of EMR and ESD has been shown to improve oncologic outcomes compared to a universal EMR program[41]. Selective resection algorithms are key to optimize specific risk-benefit profiles of various modalities, ultimately enhancing the performance of endoscopic resection as a whole.

CONCLUSION

In the minimally invasive revolution introduced by Emile and Ragheb[5], endoscopic resection has become preferred over surgery as first-line management for most large polyps based on its proven efficacy, safety, and cost-effectiveness. Recognizing this key innovation in CRC prevention and management is crucial to prevent unnecessary surgery and support iterative advances in endoscopic resection techniques.

FOOTNOTES

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