

The Difficult Colorectal Polyp



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KEYWORDS

- Colorectal polyps • Colonoscopy • Polypectomy • Endoscopic mucosal resection
- Endoscopic submucosal dissection • Laparoscopic colon surgery

KEY POINTS

- The definition of a “difficult” polyp is a moving target, but traditionally refers to polyps not amenable to endoscopic removal by the average endoscopist.
- Many patient-specific and polyp-specific factors impact the approach to difficult polyps.
- Conventional and advanced endoscopic techniques are usually successful in removing precancerous polyps with low complication rates.
- Almost 20% of polyps that are premalignant on initial biopsy will harbor an invasive malignancy that is discovered after complete resection.

INTRODUCTION

The direct relationship between neoplastic colorectal polyps and colorectal cancer has been well established.¹ Known as the adenoma to carcinoma sequence, this relationship has become the cornerstone of colorectal cancer prevention.^{2,3} Screening colonoscopy with polypectomy has been linked to a decrease in the incidence of colorectal cancer and its associated mortality.⁴⁻⁶

Of the various screening modalities available for early detection of colorectal cancer, only endoscopic polypectomy offers the ability to remove premalignant lesions before they develop into cancer. Most polyps identified at screening colonoscopy are amenable to conventional forceps or snare polypectomy.⁷ However, approximately 10% to 15% of polyps encountered at colonoscopy may be considered difficult because of their size, location, and/or morphology.⁸ These difficult polyps are the topic of this article.

Disclosures: Dr M.J. Pidala is a proctor for Intuitive Surgical. Dr M.V. Cusick has nothing to disclose.

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Surg Clin N Am 97 (2017) 515–527

<http://dx.doi.org/10.1016/j.suc.2017.01.003>

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DEFINITION OF A DIFFICULT POLYP

The definition of the difficult polyp is not well established. As implied in the name, these polyps are difficult to remove and often pose a challenge to endoscopists. As a result, patients with difficult polyps frequently require referral to a more experienced endoscopist or surgeon. These polyps are typically defined by their size, morphology, and/or location (**Box 1**). Difficult polyps are macroscopically benign, generally greater than 20 mm in size, and frequently have a flat or sessile morphology.⁹ Most are found in the right colon, where the thinner colonic wall adds a degree of complexity to polypectomy.^{10,11} These polyps may also pose a challenge when they are found wrapped around haustral folds or around sharp bends that are difficult to access.^{8,12,13} The term giant polyp has been used to describe polyps greater than 30 mm.^{14,15} Large pedunculated polyps, most often encountered in the left colon and sigmoid, also present difficulties because their removal carries increased risk of bleeding from larger vessels within the stalk.^{16,17}

In practice, what constitutes a “difficult” polyp is very subjective.¹⁸ What may appear difficult for one endoscopist may be routine for another.^{19,20} As a result, any polyp referred to another physician for removal following an initial colonoscopy may be considered “difficult.” These referrals are based on the endoscopist’s comfort, level of experience, equipment availability, and support structure. In today’s medico-legal climate, some endoscopists are unwilling to accept the risk, albeit small, of removing these larger lesions due to their increased risk of complications.^{21,22} In addition, it has been shown that the physician work required to remove these difficult polyps (>20 mm) is more than twice that for more routine polyps (<20 mm), despite minimal or no impact on reimbursement.²³ As there is ongoing pressure on physicians to maintain higher case volumes, busy endoscopists may be reluctant to manage these more difficult lesions.

Premalignant Polyps Versus Invasive Cancers

The initial goal of the endoscopic evaluation of any colorectal polyp is to localize it and determine if it contains an invasive malignancy. Histologic predictors of malignancy include polyp size²⁴ and villous histology.^{25–28} Macroscopic signs include ulceration, induration, friability, and fixation to the colonic wall. High-grade dysplasia on initial biopsy has also been shown to be an indicator of a potential underlying invasive cancer (**Box 2**).^{11,25,26,29,30}

A saline lift not only assists with polypectomy and limits associated bleeding but can also be used to identify invasive cancers. Following submucosal injection, benign adenomas are lifted off the muscularis propria. On the contrary, cancers often have fibrosis and desmoplastic reaction and will not lift with saline injection.³¹ Although

Box 1

Features of the difficult colorectal polyp

1. Macroscopically benign
2. Large (typically >20 mm)
3. Flat or sessile
4. Located around folds or kinks
5. Most in right colon or cecum
6. Large pedunculated polyps with thick stalk

Box 2**Endoscopic signs of malignancy**

- Induration
- Friability
- Fixity
- Ulceration
- Non-lifting sign

nonlifting may also occur secondary to scar from prior biopsy, the sign may be used in conjunction with other features to help predict whether a polyp harbors invasive malignancy.

Several detailed classification systems have been developed to further enhance the endoscopists' ability to determine benign from malignant lesions.^{32–34} These systems stratify the risk of underlying malignancy by assessing mucosal irregularities and various mucosal pit patterns using image-enhancing technologies, such as magnified endoscopy, chromoendoscopy, and narrow band imaging.^{35–37} These systems are not typically used in the United States, and their clinical utility is uncertain.

Despite a thorough endoscopic and histologic evaluation, 6% to 12% of difficult “pre-malignant” polyps may still contain invasive carcinoma.^{10,11,13,14} However, malignant polyps without high-risk histologic criteria may be amenable to endoscopic resection alone for cure.^{38–40} These high-risk criteria include poorly differentiated lesions, the presence of lymphovascular invasion, or surgical margins less than 2 mm.³⁰

Flat, sessile polyps harboring invasive malignancy were historically thought to be associated with a high risk of nodal metastasis as well and have been typically treated with subsequent colectomy.^{41,42} Based on work by Kudo,⁴³ flat lesions with malignant invasion limited to the superficial third or 1000 μm of the submucosa have been associated with lymph node metastasis of 0% to 3%.^{44,45} As a result, flat polyps with malignant invasion limited to the superficial third of the submucosa (<1000 μm) and no other high-risk histologic features may be treated with en bloc endoscopic resection alone.^{42,43,46,47} Malignant polyps removed by piecemeal polypectomy do not allow for adequate pathologic assessment of resection margins and should be referred for surgical evaluation.

Polyps Treated with Colectomy

Two recent studies focused on the final pathology of polyps not amenable to endoscopic removal that resulted in a colectomy.^{25,26} A 2010 study from Washington University²⁵ found that 22/165 (13.3%) had an invasive cancer on final pathology, whereas a 2012 study from the Mayo Clinic²⁶ found that 133/750 (17.7%) unresectable polyps harbored a malignancy, of which 23% were node positive. Of note, both studies found that high-grade dysplasia was a strong predictor of malignancy, with 32% to 39% of these polyps ultimately being found to contain cancer on final pathology.

NATURAL HISTORY OF UNTREATED POLYPS

In the modern era, most colon polyps are excised endoscopically or surgically, not only to prevent future growth but also to ensure diagnostic accuracy. As a result, little is known about the natural history of untreated colorectal polyps, and most

information must be gathered from studies that predated the widespread adoption of flexible endoscopy. A 1963 study analyzed more than 20,000 barium enemas and found 303 patients with polyps greater than a centimeter in size.⁴⁸ Patients were followed with serial contrast enemas for up to 128 months (mean = 30 months), and the investigators found that 20 polyps (6.6%) developed into cancer. The investigators concluded that the rates of growth for most polyps were “exceedingly slow,” and most benign adenomatous polyps could not grow into cancer throughout an average person’s lifetime. Even the fastest growing cancers reported in this study had doubling times as long as 1155 days.

A similar study from the Mayo Clinic, which predated their experience with endoscopy, was published in 1987, where 226 patients with polyps greater than 1 cm were followed with contrast enemas for a mean of 68 months (range 12–229).⁴⁹ Polyp growth was detected in only 37% of polyps, and invasive cancer was found in 9.3% at a mean of 108 months (range 24–225). The investigators estimated that the cumulative risk of malignancy at the site of the index polyp to be 2.5% at 5 years, 8% at 10 years, and 24% at 20 years. This slow rate of growth must be taken into account when recommending therapy for elderly patients or patients with significant life limiting comorbidities.

TREATMENT OPTIONS FOR DIFFICULT COLORECTAL POLYPS

Important Considerations

When considering intervention for a difficult polyp, the physician must ensure that the treatment causes less harm than good. If a polyp is thought to be premalignant, then any intervention is essentially prophylactic in nature. Therefore, a strong understanding of the polyp’s natural history, as previously outlined, must be understood and weighed against the risks of intervention. Patient age and comorbidities should impact decision making, and the treatment of a frail, elderly patient with a difficult polyp may be very different from a younger, healthier patient.

Another consideration is whether the surgery is truly “prophylactic.” As previously mentioned, many advanced polyps actually contain an invasive malignancy despite benign histology from the original biopsies. In addition, some polyps may be symptomatic, and removal will not only prevent growth but also alleviate problems such as bleeding and mucus secretion.

Polyp number and location are also important. Multiple polyps may require more invasive management than a single polyp, especially if in noncontiguous locations. Regarding location, the cecum is large and thin walled and thus more prone to perforation with advanced polypectomy. Right colectomy is also the simplest and safest location for a laparoscopic colectomy. The rectum, on the other hand, allows for local excision, plus or minus advanced techniques such as transanal endoscopic microsurgery (TEM), and tends to be more forgiving when deeper endoscopic resections are warranted. At the same time, proctectomy has significant functional implications, and a higher risk profile when compared with right colectomy.

Conventional Snare Polypectomy

Because most difficult polyps are benign, endoscopic excision should be performed whenever possible rather than major abdominopelvic surgery. When a difficult polyp exists, the first step is often a repeat colonoscopy by an endoscopist experienced in complex polypectomy,^{7,8,50} as endoscopic excision is associated with significantly lower morbidity and cost when compared with laparoscopic colectomy.^{51–53}

Conventional snare polypectomy for large difficult polyps has been reported to be safe and feasible. Binmoeller and colleagues¹⁴ reported successful snare

polypectomy without submucosal injections in 176 polyps greater than 30 mm. Malignancy was noted in 12% of polyps, and bleeding complications occurred in 24%. There were no perforations and no surgeries performed for complications. Other reports have demonstrated similar success at removing difficult polyps with conventional snare excision.^{16,54,55}

Church,⁵⁶ Voloyiannis and colleagues,⁵⁷ and Lipof and colleagues²¹ reported on patients with difficult polyps referred directly to the colorectal surgeon for resection. In all 3 studies, patients underwent repeat colonoscopy by the colorectal surgeon before any surgical resection. Successful snare polypectomy and avoidance of surgery were achieved in 32% to 74% of patients (Table 1).

Endoscopic Mucosal Resection

Advanced endoscopic resection techniques are indicated for difficult polyps that are not amenable to simple snaring. Injection-assisted endoscopic mucosal resection (EMR) or “saline lift polypectomy” was first described for rigid sigmoidoscopy in 1955 and adopted to flexible endoscopy in 1973.^{58,59} A solution is injected into the submucosal space creating a cushion that allows for snare excision of the overlying mucosa. The lifting allows for better capture of the offending mucosa and protects the deeper muscular layer of the colonic wall from thermal injury. Ideally, the abnormal mucosa is resected with a single snare excision. Alternatively, multiple injections and piecemeal resection may be necessary to completely remove the specimen. Additional techniques to assist in complete resection during EMR have been described, including cap-assisted EMR and suction-assisted EMR. These techniques use a cap that is positioned at the end of the endoscope and allows for suctioning of the desired mucosa into the cap before excision.⁵⁹

Various injection solutions have been used for EMR, and the choice is based on personal experience and preference of the endoscopist. An ideal solution should be inexpensive, readily available, nontoxic, and easy to inject while providing a sustained cushion for resection. There are currently no US Food and Drug Administration-approved injection solutions for EMR, but frequently, normal saline, hyaluronic acid, hydroxypropyl methylcellulose, succinylated gelatin, glycerol, and fibrinogen solutions are used. Dilute epinephrine (1:100,000–1:200,000) is often added to the injection solution to minimize bleeding and delay the reabsorption of the cushion.^{59,60} Some endoscopists prefer to add staining dyes, such as indigo carmine or methylene blue, to the injection solution to help discern the margins of

Table 1

Impact of repeat colonoscopy and attempted snare polypectomy to avoid surgery on patients with difficult polyps referred for resection to colorectal surgery service

| Author, Year | N | Size | Successful Polypectomy, % | Perforation | Bleeding |
|--|-----|-----------------|---------------------------|---|--------------|
| Church, ⁵⁶ 2003 | 58 | Median 45 mm | 74 | 1 (1.7%) postpolypectomy syndrome | 5.1% |
| Voloyiannis et al, ⁵⁷ 2008 | 172 | Mean 26 mm | 59 | 2 (1%) | 5% |
| Lipof et al, ²¹ 2005 | 71 | Mean 24 mm | 32 | Not reported | Not reported |

Data from Refs.^{21,56,57}

the target lesion. The coloration of the deeper layers is thought to aid in intraprocedural identification of the muscularis propria, and any associated muscular injury or perforation.^{59,61,62}

When performing EMR, en bloc resection is preferred to piecemeal polypectomy. En bloc resection allows for more accurate histologic evaluation of the entire specimen and is associated with lower recurrence rates.⁶³ A meta-analysis by Belderbos and colleagues⁶⁴ evaluated 33 studies and noted an overall recurrence rate for EMR resections to be 15%. The recurrence rate is 3% for en bloc resection and 20% for piecemeal resection.

Bleeding is the most common complication after EMR, with reported intraprocedural rates varying from 11% to 22%.^{59,63,65} The risk of intraprocedural bleeding is associated with large polyps, minimally elevated sessile polyps, polyps with villous or tubulovillous histology, and EMR performed at low-volume centers. This type of bleeding is typically managed successfully during the procedure with the use of endoclips, coagulation forceps, or coagulation with the snare tip.⁶³ Postprocedural bleeding rates have been reported to range between 2% and 11%, with clinically significant bleeding reported in 6%.^{59,63,65} The risk of postprocedure bleeding is increased with more proximal lesions, larger polyp size, and intraprocedural difficulty or complication.⁶⁵

The risk of colonic perforation during or after EMR is low, with reported rates of 1% to 2%.^{63,66} Early recognition of small perforation can be managed with endoclips.^{59,63} Late recognition or delayed perforations typically require surgical intervention.

Endoscopic Submucosal Dissection

Endoscopic submucosal dissection (ESD) was first described in 1988 for the resection of gastric lesions and adopted for the treatment of colonic lesions in early 1990s.⁶⁷ ESD involves a specialized endoscopic knife, which dissects the polyp off the muscularis propria following submucosal lifting. Compared with EMR, ESD allows for resection of larger, deeper lesions for curative intent.

The initial step in ESD includes marking the lesion to be resected and injecting a lifting agent into the submucosa at its periphery. Using the endoscopic knife, the mucosa is incised circumferentially. Additional submucosal injections are performed as necessary to lift the central portion of the lesion to allow for complete resection. There are many different commercially available devices available to perform ESD. Most of those approved by the US Food and Drug Administration are manufactured by Olympus (Olympus America, Center Valley, PA, USA) and ERBE (ERBE USA, Marietta, GA, USA). In addition to the cutting tool, hemostatic forceps are frequently used to control intraprocedural bleeding. Intraprocedural bleeding, deep resections, and small perforations recognized during the procedure can be closed with endoscopically available clips.

De Ceglie and colleagues⁶⁶ performed a systematic review of 66 studies comparing EMR and ESD, and the findings are summarized in **Table 2**. Several other meta-analyses have compared ESD with EMR, and all have demonstrated that ESD has a higher en bloc resection rate and lower local recurrence rate than EMR.^{68–70} Despite these advantages, however, ESD was reported to be more time consuming and more often required postprocedural hospitalization. In addition, ESD was also associated with higher risk of perforation (4.8%–10%).^{63,66,68}

Bleeding is once again the most often encountered intraprocedural complication associated with ESD and is reported to range from 10% to 22%.⁶⁹ When a perforation is encountered, the endoscopist should ensure the defect remains in the field of vision and clear of fluid. Endoscopic clips can be placed to seal the defect. If multiple clips

Table 2
Review comparing more than 17,900 endoscopically resected lesions by endoscopic mucosal resection and endoscopic submucosal dissection

| | EMR, % | ESD, % |
|-------------------------|---|--|
| En-bloc resection rate | 62.8 (6793/10,803) | 90.5 (5500/6077) |
| Complete resection rate | 92 (9707/10,560) | 82.1 (3743/4558) |
| Bleeding | 2.3 (270/11,873) | 2.0 (124/6077) |
| Perforation | 0.9 (109/11,873) | 4.8 (296/6077) |
| Recurrence rate | 10.4 (765/7303) overall 12.1 (131/1085) for piecemeal 3.0 (36/1187) for en bloc | 1.2 (50/3910) overall 1.2 (30/2562) for piecemeal 0.2 (5/2562) for en bloc |

Data from De Ceglie A, Hassan C, Mangiavillano B, et al. Endoscopic mucosal resection and endoscopic submucosal dissection for colorectal lesions: a systematic review. *Crit Rev Oncol Hematol* 2016;104:138–55.

are required, placement should be initiated from the lateral edge of the defect to ensure a tension-free closure. Although stricture formation after ESD is reported after esophageal and gastric procedures, stricture after colorectal ESD has not been reported.

Combined Endoscopic and Laparoscopic Surgery

Colon resection has historically been the treatment of choice for benign polyps that could not be managed endoscopically,^{25,71,72} but this premise has been recently challenged. A combined endoscopic and laparoscopic approach aims to marry the benefits of both techniques in order to safely remove precancerous polyps without a formal resection. This technique was initially described in 1993 by Drs Beck and Karulf⁷³ and has since undergone several modifications.

During this procedure, laparoscopic mobilization of the involved colonic segment is performed followed by colonoscopic snare polypectomy. The laparoscopist monitors the serosal side of the colon during the procedure and assists the endoscopist by moving and manipulating the colon to facilitate polypectomy. If concern develops for full-thickness burn or perforation, the site is repaired with laparoscopic suturing. Endoluminal insufflation often helps inspect the suture line for leaks.

Laparoscopic mobilization of the segment of colon harboring the difficult polyp helps the endoscopist better visualize and remove difficult polyps that initially may have been around folds or tight turns. In addition, the surgeon can use laparoscopic instruments to push on the serosal aspect of the colon to “present” the polyp to the endoscopist for polypectomy.^{74–76} Submucosal fluid injection to lift the polyp off the underlying muscle may aid polypectomy. If necessary, a colotomy and full-thickness excision can be performed. These combined endoscopic and laparoscopic techniques have been successful in removing 69% to 87% of benign-appearing polyps not amenable to routine snare polypectomy.^{75–83}

Another variation of combined endoscopic and laparoscopic surgery uses endoscopy to assist with a limited laparoscopic wedge resection of the colon.^{73,74,78} This technique is best used for large lesions in the tip of the cecum or around the appendiceal orifice. The cecum can be mobilized laparoscopically and surgically stapled off while under direct luminal visualization by the endoscopist. The colonoscopic view can be used to monitor the resection margin as well as intubate the ileocecal valve to assure luminal patency during cecectomy.

One of the drawbacks to laparoscopic surgery in conjunction with colonoscopy is the difficulty with visualization and manipulation of the distended colon resulting from endoscopic air insufflation.⁸⁴ Because CO₂ is rapidly absorbed from the colonic lumen, the extent and duration of colonic distension are decreased, and this is the preferred method of insufflation for endolaparoscopic cases, offering the laparoscopic surgeon better visualization and safer manipulation of the operative field.^{85,86}

Combined endolaparoscopic surgery is still in evolution, and the outcomes of relevant case series are summarized in **Table 3**. When compared with segmental resection, successful combined endoscopic and laparoscopic surgery is associated with lower morbidity, lower cost, and shorter length of hospital stay.^{51,81} Success rates range from 67% to 87%, with recurrence rates of 0% to 13%.^{75,76,79,81}

Invasive cancer has been reported in combined endoscopic and laparoscopic procedures between 0% and 11%.^{75,76,78–81} Some have recommended immediate frozen section evaluation of the polyp at the time of surgery with progression to oncologic resection for those demonstrating invasive cancer.^{74,75,77} Others have advocated a more selective approach to frozen section examinations in these cases, because of the low incidence of invasive malignancy, and the time and cost involved in frozen section.^{79,83} Ultimately, patients diagnosed with invasive cancer and high-risk features should undergo colectomy.

Transanal Minimally Invasive Surgery and Transanal Endoscopic Microsurgery

For difficult polyps located in the rectum, transanal excision is often the best approach. Transanal minimally invasive surgery and TEM are safe and effective techniques for removal of rectal polyps. These techniques are discussed in detail in D. Owen Young and Anjali S. Kumar's article, "[Local Excision of Rectal Cancer](#)," in this issue.

Surgical Resection

Historically, surgical resection has been the primary therapy for benign polyps not amenable to endoscopic removal. With the development of advanced endoscopic procedures and combined endoscopic and laparoscopic techniques, surgical

Table 3

Select series of combined endoscopic and laparoscopic surgery for difficult colon polyps

| Author, Year | N | Successful Polyp Removal, % | Invasive Cancer, % | Complications, % | Recurrence |
|------------------------------------|-----|-----------------------------|--------------------|------------------|--------------|
| Wilhelm et al, ⁸⁰ 2009 | 146 | 82 | 11 | 25 | 0.9% |
| Wood et al, ⁷⁷ 2011 | 13 | 69 | 7.7 | 15 | Not reported |
| Lee et al, ⁷⁹ 2013 | 75 | 74 | 6.7 | 9.2 | 10% |
| Crawford et al, ⁷⁶ 2015 | 30 | 67 | 3.3 | 10 | 3.3% |
| Yan et al, ⁷⁵ 2011 | 23 | 87 | 0 | 0 | 13% |
| Franklin et al, ⁷⁸ 2007 | 110 | 83 | 9 | 0 | Not reported |
| Goh et al, ⁸¹ 2014 | 30 | 73 | 6.7 | 13.3 | 0% |
| Cruz et al, ⁸⁷ 2011 | 25 | 76 | 4 | 8 | Not reported |

Data from Refs.^{75–81,87}

resection for difficult colorectal polyps should be reserved for failure or lack of availability of these less invasive approaches. When colon resection is required, a formal oncologic resection with high ligation of the feeding artery has been recommended because of the previously mentioned high incidence of invasive cancers. Most resections can be performed laparoscopically and are generally safe and well tolerated. Despite significant technical advancements in recent years, segmental colectomy is often still required to safely remove complex polyps and should remain an important tool in the surgeon's armamentarium.

SUMMARY

Advances in technology along with an improved understanding of the natural history of colonic polyps have opened the doors for many new techniques for the management of difficult polyps. Many patient-specific and polyp-specific factors must be considered. In the modern era, most premalignant polyps can be completely removed without invasive surgery. However, surgical resection is still appropriate for the most difficult lesions.

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