

Complex Colon Polypectomy

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Abstract: By interrupting the adenoma-carcinoma sequence, endoscopic polypectomy can prevent the development of colorectal cancer (CRC). Endoscopic polypectomy has, therefore, become an accepted screening and surveillance modality for CRC and has been widely adopted by clinicians, policymakers, and professional organizations as an effective screening tool. Most gastroenterologists are adequately trained to endoscopically excise the majority of polyps found in a routine colonoscopy. However, some polyps, due to their size, location, or configuration, are considered more technically challenging or are associated with an increased risk of complications (such as bleeding or perforation) and, hence, are not routinely resected. These so-called complex polypectomies are the focus of this paper.

Although colonoscopy has been performed for the last 40 years, its potential for preventing colorectal cancer (CRC) has not been recognized until the last decade. Research has shown that by interrupting the adenoma-carcinoma sequence, endoscopic polypectomy can prevent the development of CRC; therefore, endoscopic polypectomy has become an accepted screening and surveillance modality for CRC and has been widely adopted by clinicians, policymakers, and professional organizations as an effective screening tool.

Consequently, there has been a significant increase in the number of colonoscopies and endoscopic polypectomies performed annually in the United States. Currently, endoscopic polypectomy may be the most frequently performed procedure by gastroenterologists, particularly those practicing in the community setting. Most gastroenterologists are adequately trained and equipped to endoscopically excise the majority of polyps found in a routine colonoscopy, as they are frequently less than 1 cm in diameter and do not constitute a significant technical challenge to gastroenterologists. However, some polyps, due to their size, location, or configu-

Keywords

Colorectal neoplasia, colonoscopy, endoscopic mucosal resection, endoscopic submucosal dissection, postpolypectomy syndrome

ration, are considered more technically challenging or are associated with an increased risk of complications (such as bleeding or perforation) and, hence, are not routinely resected by many community gastroenterologists. This paper provides an overview of these so-called complex polypectomies. A more in-depth description of the technical aspects of difficult polypectomies can be found in several recent publications.¹⁻⁴

Definition of a Complex or Difficult Polypectomy

Although size is not the only characteristic that makes a polyp difficult to excise endoscopically, it certainly has a significant impact on the difficulty of the polypectomy. In general, sessile or pedunculated polyps more than 2 cm in diameter are considered difficult polyps. Certainly, any polyps greater than 3 cm in diameter, or so-called giant polyps, represent the most challenging polyps. Another factor that makes a polyp difficult to treat endoscopically is its location (eg, in a wall that is difficult to access with a colonoscope; within an area of severe diverticulosis; being wrapped around a fold in a clam-shell fashion; occupying more than one third of the colonic circumference; or crossing over 2 haustral folds^{1,3}).

No epidemiologic data have been reported in regard to the frequency of difficult polyps, as what may constitute a difficult polyp for one endoscopist may be a routine polyp for another, more experienced, endoscopist. However, in general, 10–15% of polyps can be categorized as difficult. Using size as the sole criterion for difficulty, the frequency of colonic polyps greater than 2 cm in diameter was 0.8–1.4% in a Japanese series,^{5,6} whereas a series by Regula and associates⁷ in Poland suggested that the frequency was higher, reporting the detection of such polyps in 5.2% of colonoscopies.

Once a large polyp is identified, endoscopists should ask themselves two questions: “Is the polyp benign?” and, if so, “Is the polyp amenable to endoscopic removal?” If there is any doubt regarding the benign nature of the polyp, or if the endoscopist does not think that they will be able to resect the polyp satisfactorily, the procedure should be aborted and the patient should be referred to a tertiary care center with expertise in endoscopic management of complex polyps to spare the patient unnecessary surgical intervention.¹

Visual inspection during colonoscopy is generally sufficient to establish whether a polyp is benign or malignant, as most polyps are benign, regardless of their size, if the following features are absent: ulceration, induration, and friability. Even so, up to 10–15% of large polyps without these features harbor invasive carcinoma.^{1,8-10}

Selection of Patients Appropriate for Endoscopic Resection

In general, a colonic polyp should be removed if it is causing clinical problems (namely, hemorrhage or obstruction), is thought to be malignant or premalignant, or its etiology is uncertain, hence requiring histopathologic evaluation for diagnosis. If feasible, the method of resection should be endoscopic, as opposed to surgical, to decrease morbidity and cost. Although there are no hard-and-fast rules, we recommend endoscopic therapy of complex colonic polyps in patients in whom the procedure can be performed safely, as assessed by the clinician, and in whom a complete resection of premalignant or malignant lesions can be anticipated (Table 1). To guarantee complete removal of a malignant lesion, it must be limited to the mucosa and submucosa and free from spread beyond the bowel wall, as assessed by imaging techniques.¹¹

Techniques Used to Perform Complex Polypectomy

Submucosal Injection and Endoscopic Mucosal Resection

The use of submucosal injection to increase the safety of fulguration of sigmoid and rectal polyps was initially introduced by Rosenberg¹² in 1955 and later by Deyhle in 1973 to raise flat mucosal lesions to facilitate ensnaring.³ Submucosal injection is now used as the basis for endoscopic mucosal resection (EMR) or mucosectomy of gastrointestinal tract lesions, including sessile and flat colon adenomas.^{2,13}

Saline or another agent is injected via an endoscopic needle under the mucosa in the area around the sessile polyp. This creates a fluid cushion that separates the mucosa from the muscular and serosal layers, resulting in a greater distance between the base of the polyp and the serosal layer. Theoretically, this decreases the risk of electrosurgical injury to the deeper structures of the intestinal wall, thus reducing the risk of colonic perforation.^{14,15} This method has become a frequent adjuvant technique in colonoscopic polypectomy and EMR, particularly in larger-sized polyps (>15 mm). For example, in a recent survey of private practice and academic gastroenterologists in the United States, 82% of respondents had used submucosal injection when performing polypectomy, though one third of them did not follow any particular rules regarding when to apply submucosal injection, and wide variability was reported with its use.¹⁶

The most frequently used agent for submucosal injection is sterile 0.9% saline, which provides adequate

Table 1. Summary of Relevant Clinical Data From Selected Series on Difficult Polypectomies Published Over the Last 10 Years

Author(s)/year	Polyps (sessile)	Size (mm)	En-bloc resection (%)	Piecemeal resection (%)	Cancer rate (%)	Bleeding (%)	Perforation (%)	Postpolypectomy syndrome (%)
Stergiou N, et al. ⁵⁵ 2003.	68 (41)	>30	38	62	12	22	0	0
Church JM. ⁵⁶ 2003.	263 (all)	>20	30	70	6	6.5	0	0.8
Doniec JM, et al. ⁵⁷ 2003.	186 (141)	>30	11	89	9	18	0.7	0
Conio M, et al. ³¹ 2004.	136 (all)	>20	0	100	13	11	0	4
Pérez Roldán F, et al. ⁵⁸ 2004.	147 (74)	>20	49	51	2.7	5.4	1.3	0
Arebi N, et al. ⁵⁹ 2007.	161 (all)	>20	0	100	2.5	4	0	2.5
Overhiser AJ, Rex DK. ⁴⁵ 2007.	184 (all)	>20	15	85	16*	7.3	1.1	0.6
Swan MB, et al. ⁴⁴ 2009.	193 (186)	10–80	34	66	5.5	3.7	0	6.4

*Including high-grade dysplasia.

lifting for 10–15 minutes. Some endoscopists prefer hypertonic saline or saline with epinephrine and/or methylene blue, as these agents have the theoretical advantage of providing longer-lasting lift, which decreases the risk of immediate hemorrhage and improves polyp demarcation. Other agents that have been used include hypertonic glucose, sodium hyaluronate,^{17,18} fibrin glue, and, more recently, hydroxy-propyl-methyl-cellulose.^{19,20}

The submucosal injection should be applied near the edge of the polyp or, at times, directly through the polyp. Injection should start at the most proximal edge of the lesion, thus avoiding difficulties with adequate visualization at the time of polypectomy.³ A sufficient amount of fluid should be injected to produce an adequate bleb that will allow for ensnaring of the polyp. Generally, 3–4 mL is sufficient, but there is no limit; some endoscopists use up to 30 mL.^{21–23} Ideally, the lesion should be resected en bloc, as this allows for a better pathologic specimen, particularly when evaluating for depth of invasion of malignant lesions (Figure 1). Unfortunately, with polyps greater than 2 cm in diameter, this is infrequently accomplished and it is often necessary to perform the polypectomy in a piecemeal fashion. As a result, adenomatous tissue can be left behind, frequently leading to lesion recurrence. To avoid recurrence, many endoscopists recommend argon-plasma coagulation ablation

of the surrounding tissue after piecemeal resection has been performed, as this procedure results in a significant reduction of adenoma recurrence.^{7,24}

Endoscopic Submucosal Dissection

Endoscopic submucosal dissection (ESD) is a more advanced form of EMR. ESD was originally pioneered in Japan for the treatment of early gastric cancer and has since been applied to the treatment of large sessile and flat neoplastic colonic lesions.²⁵ The endoscopic principles of EMR and ESD are similar, though the latter has the advantage of allowing en-bloc resection of large lesions (>2 cm), which are generally amenable only to piecemeal resection by EMR.^{26,27} After an adequate submucosal lift, ESD uses an electrosurgical cutting device or knife²⁸ to purposely dissect the deeper layers of the submucosa to remove neoplastic mucosal lesions.^{28–30} En-bloc removal is advantageous because it allows not only adequate histologic evaluation, as mentioned previously, but has also been associated with a lower recurrence rate when compared to piecemeal resection.^{31,32} A recent Japanese study of ESD in 278 patients with colorectal neoplasia described successful en-bloc resection in 90% of cases, and 80% of cases were deemed to be a complete resection. Incomplete resection was significantly associated with the location of the lesion in the right colon and the presence

of fibrosis. In this particular study, the perforation rate was 8% and was associated with large tumor size and the presence of fibrosis.³³

In a recent meta-analysis of 14 studies of ESD applied to colorectal polyps, Puli and colleagues³⁴ described the completion of en-bloc resection in 85% of cases compared to 7–34% with EMR. Although the authors support the use of ESD as the best minimally invasive endoscopic technique in the treatment of large (>2 cm) sessile and flat polyps, they do not provide information regarding complications associated with the procedure.³⁴ Also of note, this technique is not performed frequently in the United States and can sometimes take as long as several hours, making it less attractive to community gastroenterologists.^{35,36}

Complications of Endoscopic Mucosal Resection and Endoscopic Submucosal Dissection

The major risks of these techniques are perforation and bleeding. Hemorrhage is the most common complication of EMR and has been reported in 0.7–24% of cases. When occurring during EMR, hemorrhage can be classified as “procedural bleeding” and can be controlled endoscopically without further complications. Bleeding is considered “immediate” when presenting during the first 24 hours after the procedure and “delayed” when occurring more than 24 hours after the procedure.

Patients presenting with postpolypectomy hemorrhage are treated with appropriate hemodynamic resuscitation and endoscopic evaluation, generally after adequate colonic preparation with a rapid bowel purge. Once the culprit lesion has been identified endoscopically, appropriate hemostatic therapy is required.² The type of therapy used depends upon the exact location of the lesion, the presence or absence of active hemorrhage, the experience of the endoscopist, and the tools at the disposal of the endoscopist. Currently, endoclips are preferred over other modalities.

The risk of postprocedure hemorrhage may be decreased by the use of epinephrine in the submucosal injection solution used for EMR and ESD, as well as the use of primary closure of the post-EMR defect with endoclips.³⁷

The other main complication caused by EMR and ESD is colonic perforation, though most case series in the literature are usually performed in centers with a specialization in therapeutic colonoscopy and, thus, report a low frequency of such events. In a recent compilation of 17 studies of EMR for colorectal lesions, Panteris and coworkers³⁸ reported a total of 1,858 procedures with only 4 perforations (0.2%). In contrast to EMR, the risk of colonic perforation with ESD is significantly higher, at 5%, according to the same report, which compiled 7 case series of colorectal ESD procedures.³⁸

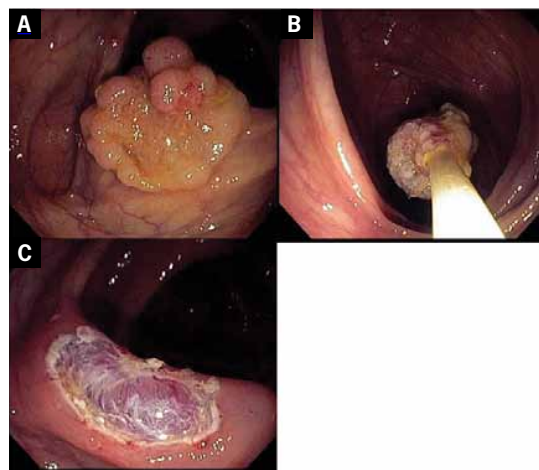


Figure 1. Successful en-bloc resection and retrieval of a large sessile polyp (A and B). Mucosal defect without bleeding or residual adenomatous tissue (C).

Treating Pedunculated Polyps

Pedunculated polyps are generally well suited for simple snare polypectomy; however, when the stalk is thick or very long, polypectomy may be technically challenging or may have an increased risk of immediate or delayed bleeding. In general, polyps with the longest pedicles tend to be located within the left colon, as the pedicles are formed by mucosa and submucosa pulled toward the lumen by the peristaltic action of the colon.

To decrease the occurrence of bleeding episodes, different approaches have been utilized, including the use of endoloops and endoclips routinely or in selected cases (Figure 2). In a recent survey of US gastroenterologists, 20% of those who completed the survey had used these techniques, though 69% of them used no specific techniques to prevent hemorrhage when removing pedunculated polyps greater than 1 cm in diameter. For those who did, the most frequent intervention was epinephrine injection at the base of the stalk.¹⁶

Kouklakis and associates³⁹ recently conducted a randomized trial of colonoscopic resection of large pedunculated polyps (>2 cm in diameter). The trial demonstrated that the combination of epinephrine injection to the base of the stalk concomitantly with endoloop placement prior to the polypectomy followed by endoclip placement resulted in a significant reduction in delayed bleeding episodes (3% vs 12.5%) compared to prepolyectomy epinephrine injection alone. Although procedure time was longer in the combination group, the reduction in bleeding episodes in the combination group resulted in a decrease in blood transfusions.

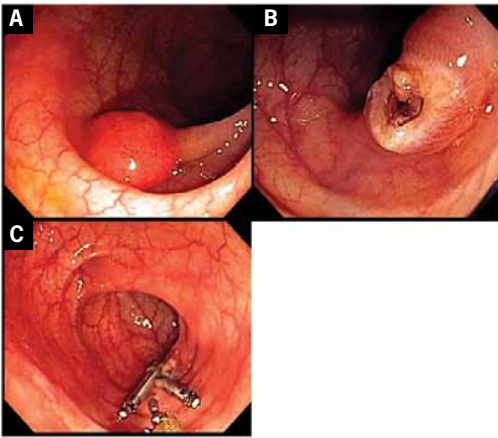


Figure 2. A pedunculated polyp with a thick stalk (A) that was successfully resected endoscopically (B). Endoclips were subsequently placed at the base of the polyp to prevent postpolypectomy bleeding (C).

In cases where the head of a pedunculated polyp is very large (>3 cm in diameter) and seemingly unable to be adequately snared en bloc, a technique known as volume reduction with epinephrine has been recently described.⁴⁰ In this technique, a solution of diluted epinephrine is directly injected into the head of the polyp to allow the vasoconstrictive effect of epinephrine to decrease the volume of the head of the polyp by up to 80%. This facilitates the ensnarement and resection of large pedunculated polyps in a single attempt, thus avoiding the problem of histologic interpretation related to the assessment of multiple fragments of colonic tissue caused by piecemeal polypectomy.⁴⁰

Retrieval of Specimens

Regardless of the endoscopic technique used to remove a large or difficult colonic polyp, it is important to retrieve as much of the removed tissue as possible to improve histologic analysis, particularly in large polyps in which the malignant potential is higher. To this end, it is recommended that polyps removed from the rectum and sigmoid be retrieved through direct endoscopic suction, using a multicompartiment trap attached to the suction connector.^{1,27} When larger pieces of the polyp have been obtained, it may be useful to transect them with a cold snare, hence facilitating the suction of now-smaller fragments. For larger polyps, particularly those located in the right colon, the endoscopist can use a Dormia basket or a Roth net, which will allow entrapment of multiple polyp fragments. When dealing with very large fragments, mul-

iple withdrawals and reinsertions of the colonoscope may be necessary to remove all of the resected tissue.⁴¹

Localization of Polypectomy Site

When managing difficult polypectomies, it is necessary not only to remove and retrieve as much adenomatous tissue as possible, but also to be able to identify the site so the endoscopist (and, occasionally, the surgeon) can readily localize it when performing surveillance colonoscopy or, in selected cases, surgically resect the lesion. To date, the best method of accomplishing this goal is to leave a tattoo in the tissue surrounding the area of interest. This is commonly achieved by submucosal injection of a permanent marker (such as India ink) or, more recently, by a commercially available sterile pure carbon surgical marker (Spot).⁴² When correctly injected into the submucosa, a blue or black bleb is created, which can be easily identified at a later date on the mucosal surface by an endoscopist and on the serosal surface by a surgeon.^{1,3}

Who Should Treat Complex or Difficult Polyps?

Patient welfare is paramount when dealing with a complex polyp. If an impending polypectomy is thought to have a high risk of complications or the endoscopist is concerned that the lesion is too large or cannot be approached in a safe manner (either because of a lack of technical expertise or necessary equipment), the procedure should not be performed. The rationale behind such a decision must be clearly discussed with the patient, and therapeutic alternatives should be provided. These alternatives include referral to a more experienced colleague, a center with more expertise in the management of complex polyps, or directly to a colorectal surgeon for consideration of definitive surgical resection. Clearly, this decision should be individualized and should take into consideration not only technical factors, but other factors such as the patient's age, their willingness to undergo multiple colonoscopies versus surgery, and the presence and severity of cardiovascular, pulmonary, or other significant comorbidities.¹

If the polypectomy attempt is aborted, we recommend that the endoscopist obtain multiple biopsies of the lesion and provide as much detail regarding the polyp as possible, acquire ample photographic and/or video documentation, and tattoo the area, as these steps will undoubtedly help in future attempts of endoscopic or surgical resection.

As demonstrated by a report from the United Kingdom, it is clear that not all physicians performing colonoscopies have the same level of expertise when dealing

with complex or large polyps. In a retrospective analysis of their 5-year experience, Brooker and coworkers⁴³ compared outcomes of endoscopic resection of large sessile polyps (>2 cm) by specialist and nonspecialist endoscopists. They reported that specialists more frequently attempted endoscopic resection of benign-appearing polyps (93%) versus nonspecialists (75%). Specialists were also better at identifying malignant polyps and referred those patients directly to surgery. Successful endoscopic management was attained in 76% of cases in the hands of specialists versus 40% in cases treated by nonspecialists. Complications were infrequent and similar among specialists and nonspecialists. The authors concluded that prompt referral to a specialist endoscopist may improve outcomes in patients with large sessile polyps by avoiding surgery or enabling complete excision during a single endoscopic session.

Based upon experiences such as these, other researchers have also advocated the creation of referral centers with endoscopists experienced in difficult polypectomies, in the hopes that this might result in a decreased need for surgical resection of complicated or large colonic polyps. One such experience from Australia was recently described. A prospective analysis was conducted of 174 patients who were referred to a specialized tertiary referral service for colonic mucosa resection and polypectomy over a 21-month period. (Two specialist endoscopists performed and/or supervised all procedures.) An established clinical pathway was followed in all cases, and similar endoscopic technique was used in all patients, most of whom underwent EMR in en-bloc or piecemeal fashion, depending upon polyp size. Among all patients who were referred, 90% avoided surgery. Excluding patients who were treated surgically due to invasive cancer, the procedural success rate was 95%. No perforations were encountered. Postpolypectomy syndrome occurred in 6.4% of patients, and clinically significant delayed bleeding occurred in 3.7% of the cases. Importantly, a cost estimate applying Australian cost parameters, and assuming that all these patients had been treated surgically, resulted in a total medical cost savings equivalent to nearly \$7,000 per patient.⁴⁴

In a recent publication, Overhiser and Rex⁴⁵ described their experiences in regard to the work and resources needed for the endoscopic resection of large sessile colorectal polyps, compared to small polyps, in terms of physician time, equipment use, and cost. In over 180 patients with large polyps compared to a similar number of patients with small polyps, the procedure time was significantly longer in the former group (51.4±25.6 minutes vs 20±8.6 minutes). The large polyp group also required much more equipment to complete

the polypectomy, resulting in an average equipment cost of \$307 compared to \$35 in the control group. Another major difference included complication rates, as none of the control group patients developed complications compared to the large polyp group, which had 2 perforations (1.1%), 1 postpolypectomy syndrome (0.6%), 13 cases (7.3%) of delayed postpolypectomy bleeds, and an overall hospitalization rate of 6.2%.⁴⁵

Surgical Resection

If a colonic polyp is not amenable to endoscopic resection, or the patient is not willing to undergo serial endoscopies, the next modality to consider is definitive surgical resection.⁴⁶ In recent years, the advent of laparoscopic and minimally invasive surgery has certainly made this alternative much more appealing.⁴⁶⁻⁴⁸ This approach is associated with improved postoperative recovery and morbidity, with oncologic outcomes similar to those associated with open colectomy, at least in the setting of CRC.⁴⁹

Not all patients referred to a colorectal surgeon for surgical resection of a complex or large polyp warrant such treatment. Experienced colorectal surgeons generally prefer to perform the colonoscopy themselves; in many cases, they can treat the polyp endoscopically,^{50,51} and if they cannot, they are still able to directly assess the polyp and tattoo the appropriate site prior to surgery. As an example, in a recent report of their experiences with repeat colonoscopy in patients referred for surgical treatment of difficult polyps, Voloyiannis and colleagues⁵² were able to successfully resect the problematic polyp in 58% of cases, thus avoiding major surgery in these patients.

Some groups have recently advocated the use of combined laparoscopic and colonoscopic approaches to the treatment of difficult colon polyps in carefully selected patients. Several combinations of laparoscopic-endoscopic "rendezvous" procedures have been established, including laparoscopically assisted endoscopic transluminal resection, endoscopically assisted wedge or anatomical resection, and intraoperative tumor location by colonoscopy for adequate oncologic margins at the time of laparoscopic colectomy with curative intent.^{53,54} These approaches are not currently in widespread use in clinical practice.

Summary

Complex polypectomies require not only expertise on behalf of the endoscopist, but also sufficient time, appropriate accessories, and knowledgeable ancillary staff. These procedures should be pursued by specially trained physicians, as they are more technically challenging than routine polypectomies. Judicial use of this approach

can lead to a decrease in the need for surgical resection of difficult polyps, resulting in improved morbidity and mortality and a reduction in medical costs.

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