Colonoscopy: Advanced and Emerging Techniques-A Review of Colonoscopic Approaches to Colorectal Conditions.

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Colonoscopy: Advanced and Emerging Techniques—A Review of Colonoscopic Approaches to Colorectal Conditions

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Abstract

Keywords
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► endoscopic submucosal dissection
► chromoendoscopy
► colonic stents

A complete colonoscopy is key in the diagnostic and therapeutic approaches to a variety of colorectal diseases. Major challenges are incomplete polyp removal and missed polyps, particularly in the setting of a difficult colonoscopy. There are a variety of both well-established and newer techniques that have been developed to optimize polyp detection, perform complete polypectomy, and endoscopically treat various complications and conditions such as strictures and perforations. The objective of this article is to familiarize the colorectal surgeon with techniques utilized by advanced endoscopists.

Maximizing Polyp Detection Rates

Navigating the Difficult Colon

Briefly, the elementary tips in colonoscopy include avoidance of pushing against resistance, recognizing and reducing loops, use of CO₂ insufflation when possible, and anticipation of the difficult case. Past medical history of substance abuse or previous high sedation requirements may provide insight on how to sedate the patient adequately for a successful exam. Useful maneuvers for patients with redundant, tortuous colons include stiffening the scope, use of abdominal
pressure, and manipulation of patient positioning. As surgeons, we often need to perform colonoscopy on patients who have had prior abdominal surgeries. For this group, we may need to consider using more flexible scopes such as upper endoscopes, enteroscopes, or pediatric colonoscopes. Additional techniques exist including the use of water immersion, overtubes, and caps.

**Advanced Imaging Techniques**

With the concern for missed adenomas leading to interval cancers, various new endoscopic imaging techniques have been developed to perform more precise examinations. These include high-definition imaging, chromoendoscopy, narrow band imaging (NBI), and use of retroscopes.

**High-Definition Imaging**

High-definition colonoscopy involves a high-definition monitor, which shows more images per second and provides higher resolution imaging. There have been various studies evaluating adenoma detection rates of high-definition colonoscopy compared with standard white-light endoscopy. A retrospective study of 2,430 patients showed significantly higher adenoma detection with high-definition endoscopy, although this mainly concerned smaller lesions. Other studies have shown no significant difference in adenoma or polyp detection rates.

**Chromoendoscopy**

Chromoendoscopy involves applying contrast dyes to enhance mucosal abnormality detection. The types of contrast dyes used in colonoscopy include methylene blue, which is actively absorbed by the mucosa, and indigo carmine, which highlights abnormal tissue by pooling in mucosal irregularities. Debris is washed away and glucagon is administered to minimize gut contraction. The dye is typically sprayed on the mucosa via the working channel of the colonoscope. This is repeated segmentally during withdrawal of the scope. This adds time to the procedure, and its efficacy depends on the operator’s ability to identify abnormalities. The Kudo classification system groups surface pit-patterns, allowing for the estimation of the malignant potential of the lesion.

Although studies have not shown a significant increase in adenoma detection rates during its use in routine colonoscopy, chromoendoscopy may have a role in detection in high-risk populations, such as those with ulcerative colitis or familial polyposis. Various studies, both with indigo carmine and methylene blue, show a stronger correlation between endoscopic assessment and histological findings with staining in patients with ulcerative colitis. Matsumoto et al compared chromoendoscopy to white light and NBI for detection of diminutive lesions in patients with familial adenomatous polyposis, showing higher sensitivity of chromoendoscopy in detection of diminutive lesions at all sites of the colon. Nevertheless, the absolute role for chromoendoscopy in surveillance of patients with inflammatory bowel disease, much less other high-risk populations such as those with familial adenomatous polyposis or risks for hereditary nonpolyposis colon cancer, is not well established.

There may be a role for chromoendoscopy in the assessment of the adequacy of resection margins after EMR or ESD. One study described sensitivities with chromoendoscopy to predict remnant tissue in lateral and deep margins after mucosal resection of 79 and 80%, respectively. Overall, chromoendoscopy may play a role in the surveillance of
IBD, although uniformity of optimal staining techniques and analysis of mucosal surface patterns is required.\(^3\)

**Narrow Band Imaging**

Narrow band imaging is a newer technology than chromoendoscopy and is otherwise known as “virtual chromoendoscopy.” Optical filters within the light source of the endoscope are used to narrow the bandwidth of the light, precluding the need for time-consuming application of a contrast dye. NBI (Olympus, Tokyo, Japan) narrows the red light, thereby decreasing penetration depth and resulting in a green-blue image that accentuates the mucosal vasculature and surface pattern morphology. The specific wavelength corresponds to the peak absorption spectrum of hemoglobin. One limitation is the darker image overall, which may limit evaluation of the colonic structures, and also prints poorly on reports. Stool and bile also interfere with visualization. Various meta-analyses have not found significant improvement of polyp detection with NBI when compared with white-light endoscopy.\(^19\)

Similarly, no significant difference was found in adenoma detection in high-risk patients, such as those with ulcerative colitis, when comparing NBI with conventional endoscopy.

Other forms of virtual chromoendoscopy include Fujinon intelligent color enhancement (FICE) and auto fluorescence imaging (AFI). FICE (Fujinon Inc., Wayne, NJ) involves a spectral estimation technology that also narrows the bandwidth of light. There are few randomized studies, and images can also be dark. AFI utilizes short wavelength light, leading to excitation of endogenous substances and emission of the autofluorescent light. Neoplastic tissue appears red and non-neoplastic tissue is green. It has a lower adenoma miss rate compared with white light colonoscopy but has lower resolution of images.\(^6\) Overall, the literature suggests that virtual chromoendoscopy only provides minor benefit to detection of small and flat lesions. Limitations of these techniques call for improvement of devices that can provide brighter images.\(^6\)

**Retrosopes**

The Third Eye Retroscope (Avantis Medical Systems, Sunnyvale, CA) was introduced in 2007. It consists of a 3.5-mm fiber optic catheter that is introduced through the working channel of the colonoscope. The retroscope turns 180 degrees and projects two images on one monitor, one of which is a 135-degree retrograde view. This allows for views behind proximal folds. One multicenter study showed the Third Eye improved additional lesions detection rates for lesions 6 mm or larger and 10 mm or larger at 25 and 33%, respectively.\(^20\) Those polyps were subsequently removed after localization with the standard view.

A limitation of the Third Eye is that the working channel is blocked, necessitating removal of the device before introducing polypectomy instruments. Similarly, the suctioning capacity is reduced by 50%, requiring that thorough suctioning be performed during insertion of the scope.

Slimmer colonoscopes called “RetroView” devices were developed to allow for distal tip retroflexion up to 210 degrees and additional capabilities for chromoendoscopy techniques using available working channels. This allows for visualization and endoscopic therapy without removal of devices. There is no scientific evidence regarding these newer devices at this time.

Finally, newer devices like the G-EYE endoscope (Smart Medical, Ra’anana, Israel) and Full Spectrum Endoscopy (FUSE; EndoChoice, Alpharetta, GA) were developed to maximize adenoma detection. G-EYE works on withdrawal by utilizing a permanent balloon on the end of the colonoscope that inflates in the cecum, thereby flattening folds and stabilizing the endoscope on withdrawal.\(^21\) FUSE allows for a high-resolution 330-degree view of the lumen using a colonoscope with three images and LED groups on the front and both sides of the flexible tip. The three views are projected on three monitors and theoretically provides for a more comprehensive view, particularly near flexures and

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**Fig. 1** Chromoendoscopy helps delineate the borders of (A) a sessile polyp with high-grade dysplasia and (B) a dysplasia-associated lesion or mass in ulcerative colitis (photo credit: Michael Chiorean).
behind folds. Early studies show lower adenoma miss rates with FUSE compared with standard colonoscopy, but more studies are required before definitive conclusions can be made. 

Overall, the aforementioned innovations have shown little additional diagnostic yield in light of the longer procedure times. The optimal visualization technique would enhance the view of whole colonic mucosa while maintaining the capability to simultaneously wash, suction, and perform polypectomies in a practical and time-efficient manner. The ultimate goal is to enhance the diagnostic yield of colonoscopy.

**Therapeutic and Advanced Endoscopic Techniques**

**Complex Polypectomy**

The difficult polyp can be defined by a range of variables, including the number of polyps, a size greater than 15 mm, a certain shape whether with a large pedicle or flat appearance, or difficult location, such as behind a fold or in the cecum. Large polyps were historically approached by surgery, with its inherent complication and morbidity rates.

EMR and ESD are techniques to consider when the use of biopsy forceps or snare is not optimal. EMR and ESD are valid and safe alternatives to an operation, while minimizing complication rates and cost.

Besides being aware of the options of standard polypectomy, EMR and ESD, the physician needs to know indications for each technique. NBI can be used to decide if the lesion is amenable to endoscopic resection, such that it only extends to the mucosa or <1,000 µm into the submucosa. Laparoscopic-assisted endoscopic polypectomy can also be used for more challenging polyps and will be discussed separately in another article in this issue. Finally, surgery should be considered if there is suggestion of deep invasion.

**EMR/ESD Overview**

The resection plane for both EMR and ESD is the superficial submucosal layer. In contrast, standard polypectomy resects at the mucosal level. Both techniques utilize an injection into the submucosal layer. The injectate can be normal saline (with or without epinephrine), hypertonic solutions such as glycerol, or colloid-based solutions, such as hydroxyethyl starch. The normal saline lift often lasts for approximately 10 to 15 minutes, with longer lifts reported with other injectates. Addition of indigo carmine into the injectate helps delineate the borders of the polyp being readied for endomucosal resection or endoscopic submucosal dissection (Fig. 2). A volume of 3 to 4 mL is usually sufficient, although in some cases repeated withdrawals and reinsetions of the colonoscope may be required. The edges of the resection can be coagulated (Fig. 4). The site of resection should be tattooed with India ink or a sterile pure carbon surgical marker to localize the site for surgical resection or surveillance colonoscopy.

As described later in this section, there are advantages and disadvantages to both EMR and ESD. Both approaches have overall similar colon-preserving efficacy. In addition, EMR and ESD can be safely performed for lesions in challenging areas such as the ileocecal valve, appendiceal orifice, or dentate line. Surgery should be reserved for those lesions that extend through the valve or into the appendiceal orifice. Regarding follow-up after these successful EMR/ESD techniques, repeat endoscopy should be performed every 1 to 3 years.

Once the lesion is resected by either technique, retrieval is essential to optimize histological analysis. Whether performed en bloc or piecemeal, the polyp can be retrieved using a net or basket (Fig. 3), although in some cases repeated withdrawals and reinsetions of the colonoscope may be required. The edges of the resection can be coagulated (Fig. 4). The site of resection should be tattooed with India ink or a sterile pure carbon surgical marker to localize the site for surgical resection or surveillance colonoscopy.
EMR involves a “lift-and-cut” technique, during which the injectate is infused while moving the needle to create a protective cushion. If the lesion is smaller than 20 mm, it may be encircled with the snare as a whole. The snare is lifted from the wall, loosened briefly to release entrapped muscularis propria, and then transected with blended current. Larger lesions may require piecemeal resection. For these resections, the free margin of the lesion is the start point for subsequent resections until the lesion is completely resected. EMR is typically used for lesions up to 20 mm in size, although the piecemeal resection for lesions greater than 20 mm has helped patients avoid surgery in up to 90% of cases.

3 months for the first 2 years after piecemeal resection and every 3 to 6 months during the first 2 years after en bloc resection.27

Endoscopic Mucosal Resection

EMR involves a “lift-and-cut” technique, during which the injectate is infused while moving the needle to create a protective cushion. If the lesion is smaller than 20 mm, it may be encircled with the snare as a whole. The snare is lifted from the wall, loosened briefly to release entrapped muscularis propria, and then transected with blended current. Larger lesions may require piecemeal resection. For these resections, the free margin of the lesion is the start point for subsequent resections until the lesion is completely resected. EMR is typically used for lesions up to 20 mm in size, although the piecemeal resection for lesions greater than 20 mm has helped patients avoid surgery in up to 90% of cases.22,23 For those skilled in these techniques, EMR can successfully treat most colonic lesions, whether en bloc or piecemeal, with only approximately 3 to 10% requiring surgery.28

The concern with this approach is the recurrence rate. Studies have described higher adenoma recurrence rates with EMR of larger lesions, in up to 25% of cases.22,29 These lesions are usually greater than 20 mm and even larger than 40 mm. Other predictors include piecemeal resection in six or more pieces and the use of argon plasma coagulation.23 The additional challenge is the inherent suboptimal pathological evaluation of a piecemeal resection. Preferably, an en bloc resection provides for the assessment of both horizontal and deep margins, which is not possible with a piecemeal resection.

To detect these recurrences, a follow-up endoscopy was performed 3 to 6 months after the initial EMR and most recurrences were already visible by then.30 To reduce the recurrence rate, some apply argon plasma coagulation to the borders of resected areas. EMR has been noted to be ineffective for certain larger lesions. Factors associated with these failures include previous resection attempts, location in the proximal colon or ileocecal valve, submucosal carcinoma, or a nongranular lateral spreading tumor quality.31

Along with the lift-and-cut technique, cap-assisted EMR has been described but recommended for rectal lesions only, given the high risk of perforation in other areas of the colon. As described earlier, the plastic cap on the tip of the scope provides better visualization by flattening folds and the improved ability to resect lesions at whatever position they are found. The use of cap-assisted EMR has been limited by concerns for aspirating the muscularis propria, which could lead to perforation. Conio et al resected 146 sessile polyps and 136 lateral spreading tumors with cap-assisted EMR with post-polypectomy bleeding complications in 7%, all of which were controlled endoscopically.32 There were no perforations, and endoscopic follow-up showed 4% recurrence at 12 months which were treated with resection and/or ablation. The main limitations were inherent to EMR with a piecemeal fashion resection and limitations to histological evaluation. Even without actual suction, applying pressure of the cap on the lesion allowed for adequate protrusion and therefore improved “control” of aspirated tissue, minimizing the risk of perforation.

Endoscopic Submucosal Dissection

ESD was created to counter the shortcomings of EMR. The submucosal injection is performed at the proximal border of the lesion, after which endoscopic knives are used to create an incision and dissect the submucosal layer free. This is performed first on one-half of the lesion then repeated on the other side to resect the lesion en bloc. Similarly, ESD can be performed by creating an incision circumferentially with dissection to the base of the lesion, followed by snare resection of the remainder of the lesion.33 ESD is informally indicated for lesions larger than 20 mm, when high-grade dysplasia or superficial submucosal invasion is suspected, and when other endoscopic techniques have failed. Repici et al performed a meta-analysis showing ESD as a highly effective method for the management of lesions larger than 20 mm and for post-EMR recurrences.34 The R0 resection rate was 88% in this study.

Clips are useful in closing the defect after ESD. When a thick stalk is involved, a detachable Endoloop placement may help in prophylactic control of bleeding after ESD, as these thick stalks often contain large vessels. Compared with EMR, ESD is time consuming and has a higher rate of perforation. However, it has an en-bloc removal with a lower recurrence rate than EMR, especially for larger lesions.35

Complications

The general risks of colonoscopy include bleeding, perforation, and post-polypectomy syndrome. These can often be managed conservatively or endoscopically, if necessary. Surgery is a rare but known requirement for certain cases. The majority of complications occur after polypectomy, particularly when electrocautery is used.36 Electrocautery is utilized in all modalities of polypectomy whether conventional, EMR, or ESD. In general, electrocautery should be avoided in removal of small polyps. Identified risk factors for complications, even with cold forceps or snare polypectomy, include
multiple polypectomies, polyp size, right-sided lesions, inexperience of the endoscopist, and patient age.\textsuperscript{37}

Bleeding is the most common complication and can occur immediately or up to 3 to 4 weeks post-polypectomy.\textsuperscript{36} Most are self-limiting or easily treated with clip placement or epinephrine injection. Prophylactic use of clips or coagulation for preventive measures is not effective.\textsuperscript{38}

The bleeding risk for EMR and ESD are roughly similar, whether immediate or delayed, with a reported incidence of 1 to 10%.\textsuperscript{33} Repici et al reported a bleeding rate of 2% for ESD with all cases treated endoscopically.\textsuperscript{34} Piecemeal resection and previous resection attempts were not found to increase the risk of bleeding.\textsuperscript{39} Clip placement after EMR did seem to provide protection in a retrospective study.\textsuperscript{40} Large pedunculated polyps, which may have several feeding vessels, may have increased risk of bleeding. Prophylactic use of clips, Endoloops, or epinephrine injection of the stalk may reduce this risk. Other reported risk factors in those with resection of large pedunculated polyps include older age, size and histology of the polyp, stalk diameter, and use of anticoagulation medications.\textsuperscript{41}

Perforation is the second most common complication after polypectomy. EMR and ESD are associated with higher perforation rates. The reported rates of perforation for EMR are 0 to 1.5\%\textsuperscript{22,23,42} For ESD, perforation rates have ranged from 1.5 to 10% in the literature, with overall rate of 5%.\textsuperscript{33,34} The rate of perforation tends to decrease with more experience, but lesions greater than 50 mm or those of nongranular laterally spreading tumor morphology tend to increase the risk of perforation in ESD. Lesion location in the right colon, where the wall is thin, also increases this risk.

Most perforations with EMR or ESD can be treated endoscopically with clips. Few require surgery.\textsuperscript{23} Use of the over-the-scope clip has been reported for ESD-related perforation.\textsuperscript{43} Due to the relatively large polypectomies performed using EMR and ESD techniques, there is also concern of stricture formation postprocedure, yet this is a rare occurrence. The general approach and management of these complications will be discussed later in this article. Lastly, polypectomy-related mortality after EMR or ESD is nearly zero.\textsuperscript{44}

\section*{Approach to Strictures}

\subsection*{Colonic Stents}
There are many reports regarding the benefit of self-expanding stents for palliation of unresectable colorectal cancer or as a bridge before surgery. Stents provide low complication rates with increased quality of life.\textsuperscript{45,46} The risks of stents include migration rates of up to 11.8\%, occlusion rates of up to 12\%, and perforation rates of up to 4.5\%.\textsuperscript{47}

A recent study by Kim et al shows that these stents can also be a first-line treatment option for those with colorectal obstruction secondary to a noncolonic malignancy with peritoneal carcinomatosis.\textsuperscript{48} Examples of such causes include extrinsic compression, extrinsic invasion, adhesions, and motility dysfunctions due to peritoneal carcinomatosis. Overall clinical success was achieved in 50\%, and 55\% did not require a surgical intervention during the follow-up period. Because these patients did not have a definitive luminal tumor, uncovered stents were used in most cases, thereby lowering the rate of stent migration. The authors concluded that stent placement in these patients may help avoid surgical approaches and provide a bridge to optimize quality of life while pursuing medical management. Lastly, stents can be used in the management of Crohn stricture (\textsuperscript{\textbullet}Fig. 5A, B).

\subsection*{Balloon Dilatation}
Intestinal strictures occur at the level of an anastomosis after resection and are a major cause of morbidity, especially among patients with Crohn disease. In anastomotic strictures in patients without Crohn disease, prospective studies showed few complications after dilation, whereas complications after dilation in Crohn disease–related strictures can reach up to 18\%, with almost all being perforations.\textsuperscript{49} In the Crohn group, strictures likely arise from chronic inflammation with abnormal healing. They can occur anywhere in the gastrointestinal tract but most often affect the terminal ileum, ileocolonic anastomosis, and rectum. Historically, the treatment of strictures involved surgical resection or strictureplasty. Endoscopic balloon dilation provides an

\begin{figure}[h]
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\includegraphics[width=\textwidth]{Fig_5.png}
\caption{Before (A) and after (B) the use of self-expanding stents in Crohn stricture (photo credit: Richard Kozarek).}
\end{figure}
alternative to surgery and is found to be particularly successful in short-length strictures (►Fig. 6A, B). A standard colonoscope is used with a 10 to 20 mm through-the-scope balloon. The patient can experience immediate resolution in more than 80% of cases but will often require repeat dilation until the colonoscope can traverse the affected area.49,50

A recent retrospective cohort study by Greener et al compared short- and long-term outcomes of balloon dilation versus surgical resection in patients with symptomatic fibrostenotic Crohn disease. The endoscopic balloon group required reinterventions in 40% compared with 10% of those in the surgical group. Although surgery involved higher cost and longer hospitalizations, the long-term outcomes after operative intervention exceeded those of endoscopic dilation.51 Nevertheless, there are subsets of patients who may benefit from dilation including those with malnourishment or those with short bowel syndrome.

Approach to Perforation

The incidence of perforation during colonoscopy ranges from 0.05 to 0.39% with risk factors including older age, female gender, comorbidities, history of diverticulitis, and previous polypectomy.52 The mechanisms of perforation include blunt trauma, excessive thermal injury, and unintentional endoscopic resection. Perforations from blunt trauma tend to be large in size and involve the rectosigmoid. Unintentional injuries sustained during polyp resection tend to be smaller and most commonly in the right colon. Thermal injuries can also be small but may not be detected until after completion of the procedure.

Perforations can be identified by direct visualization of the mural defect or by visualization of an intra-abdominal organ or fat. Clinically, the patient may exhibit tachycardia, tenderness, or abdominal pain. Radiographically, plain films may show pneumoperitoneum in cases of perforations at the antimesenteric surface. Mesenteric perforations may present with air in the retroperitoneum, and these may be able to be managed with medical intervention alone (admission, intravenous antibiotics, nil per os, observation, serial abdominal exams).

With advanced techniques for polyp resection such as ESD, the perforation risk has been reported to be up to 10% with risk factors including larger size, evidence of submucosal fibrosis, lateral tumor spread, or location in the cecum and ascending colon.53,54

Surgical intervention has been the mainstay of perforation management. It is still indicated in cases of large perforations, generalized peritonitis, and concomitant colorectal pathology. Nonsurgical approaches are feasible in many cases with the use of hemoclips and over-the-scope clips. It is prudent to know of endoscopic options for perforation closure and to know when these approaches can be safely utilized.

Hemoclips

Through-the-scope clips have been successfully used to manage small perforations, as in the case of perforations after EMR or ESD. A variety of clips exist including standard and three-pronged clips (TriClip; Cook Medical, Winston-Salem, NC). Some clips can reopen and close up to five times before deployment (Resolution Clip, Boston Scientific, Natick, MA), allowing for readjustment and precise placement.

Ovesco Clips

Over-the-scope clips (Ovesco Endoscopy, Tübingen, Germany) are a more recent addition, which may be useful for larger perforations.55 A case series showed successful closure of perforations up to 30 mm in size.56 Of the nine cases, six improved without further intervention, whereas three required laparoscopy after development of peritonitis. When endoscopic closure is unsuccessful, patients may require surgical intervention.

Conclusion

Colon and rectal surgeons typically have markedly less time than gastroenterologists to spend in the endoscopy suite. Therefore, it is imperative that those who wish to perform lower intestinal endoscopy be familiar with tips and tricks to
maximize safety and quality during their examinations. In addition, they should keep up with advanced techniques which allow optimization of polyp detection, execution of complete polypectomy, and endoscopic treatment of various complications and conditions, such as strictures and perforations. Resources such as video tutorials, product brochures, and review articles such as this one can help with this effort to maintain proficiency and familiarity.

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