



Colonoscopic polypectomy

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Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Colonoscopy serves as a diagnostic and therapeutic modality for colorectal cancer screening, as well as treatment for precancerous lesions and even early carcinoma. The management of colorectal polyps is founded upon the adenoma-carcinoma sequence, which provides insight as to how colorectal cancers are developed through a series of genetic dysregulations. Endoscopic polypectomy techniques are widely employed in the everyday clinical setting. This article provides an overview of different polypectomy techniques, complications, and surveillance after polypectomy.

Keywords: Colonoscopy; polyps; polypectomy

Received: 01 July 2019; Accepted: 14 August 2019; Published: 25 September 2019.

doi: 10.21037/ales.2019.08.09

View this article at: <http://dx.doi.org/10.21037/ales.2019.08.09>

Introduction

Colorectal cancer is the second leading cause of cancer related deaths in the United States. In 2016, 67.3% of U.S. adults aged 50–75 years were up to date with their colorectal cancer screening and 25.6% had never been screened. For adults without health insurance, only 36.3% have been screened (1). The American Cancer Society currently recommends colorectal cancer screening starting at age 45 for patients who are average risk (2). Colonoscopy serves as a diagnostic and therapeutic modality for colorectal cancer screening. Endoscopic polypectomy techniques are widely employed in the everyday clinical setting. This article provides an overview of different polypectomy techniques, complications, and surveillance after polypectomy.

Classification

Polyps are classified on their gross appearance and histologic diagnosis. Histologic types of colon polyps are adenomas, sessile serrated adenomas, hyperplastic, hamartomas, and inflammatory. Adenomas account for 60–70% of polyps

identified during colonoscopy (3). Adenomas are further defined by the percentage of villous component as tubular, tubulovillous, and villous. Almost 90% of polyps identified during colonoscopy are less than 10 mm with polyps in this group being divided further into <5 and 6–9 mm. Ponugoti *et al.* reported the largest series with polyps less than 10 mm where high grade dysplasia was found in 0.3% of polyps <5 mm and 0.8% of polyps 6–9 mm (4). Invasive cancer was not identified in any polyp less than 10 mm. Even though there is a current discussion regarding remove and discard for diminutive polyps, standard of care remains that colon polyps be resected by the safest technique once identified.

Adenoma detection rate (ADR)

The ADR is a well-recognized quality indicator for colonoscopy (5,6). The ADR is defined as the number of screening colonoscopies where at least one adenoma is removed divided by the total number of screening colonoscopies performed by the endoscopist (7). The minimum number of colonoscopies needed to calculate an accurate ADR with a tight 95% confidence interval

is 500 (8). Serrated adenomas are not included in the calculation of the ADR. The American Society of Gastrointestinal Endoscopists and the American College of Gastroenterology include ADR in their quality metrics for colonoscopy with a level of evidential support of 1C (9). ADR minimal benchmarks for men and women are 30% and 20%, respectively.

ADR varies significantly between providers conferring decreased interval cancer risks and mortality for patients who have a colonoscopy performed by a provider with a high ADR. ADR is a composite measure that accounts for withdrawal time, prep quality, and technique influencing the initial surveillance recommendation after screening colonoscopy as well as the detection of interval cancers. Endoscopist variability in identifying polyps, ensuring complete removal, and surveying the entire colon account for the majority of interval or post-polypectomy cancers (10,11). Corley *et al.* evaluated the ADR for 223,842 patients who underwent 264,792 colonoscopies by 136 endoscopists (6). For each 1% improvement in the ADR, a 3% decrease in colorectal cancer incidence and a 5% decrease in mortality was noted.

Polypectomy techniques

Forcep polypectomy

While polypectomy techniques are variable in current practice, a standardized survey interviewing 285 practicing gastroenterologists revealed that cold forceps polypectomy is the most commonly employed technique for diminutive polyps 1–3 mm in size (12). The polyp is grasped with standard or jumbo forceps that exit the channel of a therapeutic colonoscope at the 5 to 7 o'clock position and the forceps removed with the lesion in the jaws of the forceps (13). Cold forceps polypectomy is limited to the removal of small polyps ≤ 5 mm and can result in an incomplete resection rate as high as 61% (13,14). Hot forceps polypectomy is similar to cold, with the utilization of electrocautery to fulgurate residual lesion on the colonic mucosa (13).

Snare polypectomy

Snare polypectomy has been established as a safe and effective technique for resection of small colorectal polyps ≤ 10 mm in multiple studies (12,15,16). A snare device is passed through the working channel of a colonoscope

and a metal ring deployed over the polyp (13). Once the polyp, along with 2 mm of healthy colonic mucosal margin is captured, the snare is closed until the base of the polyp is cut. Any bleeding at the base of the lesion is generally self-limiting. For snare electrocautery, the snare should be closed slowly, while the polyp is pulled away from the colonic mucosa to avoid deep thermal injury (13).

The current paradigm shift in endoscopic management of small colorectal polyps favors cold snare instead of hot snare polypectomy (13). A meta-analysis of 12 studies involving 2,481 patients who had polyps less than 10 mm removed with either hot or cold snare polypectomy demonstrated no statistical difference for complete resection rate and bleeding needing treatment. The hot snare polypectomy group had significantly longer total colonoscopy and polypectomy times (16).

There is only one systematic review and meta-analysis evaluating cold snare polypectomy for polyps greater than 10 mm (17). Eight studies with 522 polyps conducted between 2014 and 2018 were included with the mean polyp size of 17.5 mm. The overall intra- and post-procedure pooled bleeding rates were 0.7% and 0.5%, respectively. For polyps >20 mm (n=132) the intra-procedure pooled bleeding rate was 1.3% and there were no post-procedure bleeds. The pooled complete resection rate for all polyps was 99.3%.

Advanced polypectomy techniques

Endoscopic mucosal resection (EMR)

EMR generally refers to the technique of submucosal injection of a polyp followed by snare polypectomy (18). Submucosal injection technique can be considered prior to the polypectomy to create a submucosal cushion, assisting in the complete resection of the lesion. Saline is widely used for the submucosal injection since it is cheap and readily available. Diluted epinephrine (concentration of 1:100,000) is often added to promote hemostasis. Indigo Carmine or methylene blue, in a 0.04% concentration, can be added as well providing definition to the borders of the polyp and identification of the submucosal plane (19). Other submucosal injectable agents include hyaluronic acid, hypertonic saline, hydroxypropyl methyl cellulose, fibrinogen and glycerol. These agents are expensive, difficult to prepare, activate an inflammatory response, and challenging to deliver (20,21).

The goal of EMR is an en bloc resection using a precise

injection technique to raise the lesion into the lumen and closer to the colonoscope. If that is not achievable, the polyp should be removed in as few sections as possible. The colonoscope is manipulated such that the polyp is placed at the 5 o'clock position where the instrument exits the working channel, and the injection needle penetrates the polyp proximally and perpendicularly just 2–3 mm behind the polyp. If a polyp is located at an area of angulation or draped across a fold, inject and resect the most challenging section of the polyp first (19). A well-placed injection will lift the mucosa while an extramural injection will cause no change in the mucosa. The volume of fluid needed to adequately lift a polyp is dependent on its size. Larger polyps may be approached with a series of sequential injections and resections (19). Follow up colonoscopy is recommended within 4–6 months of the procedure and then yearly for 3 years (19).

While EMR provides a safe way of avoiding deep thermal spread to the colonic wall when using electrocautery to resect large polyps, it has several limitations (20,21). Intra-procedure bleeding occurs in 11% of EMR cases when the polyp is greater than 20 mm (22). Bleeding can be controlled by snare tip cautery and clips. The post-procedure bleeding rate for these larger polyps is 6.2–7%, usually occurs within the first 48 hours, and is associated with right-sided lesions, increasing polyp size, and technical difficulties (22,23).

The perforation rate associated with EMR is 1–2% (24). Injury to the muscularis propria can be identified by a “target sign” on the resection side of the specimen and its mirror image in the colonic resection bed (25). A target sign consists of a circle with a white circumference, mucosa, and piece of muscularis propria in the middle. Clips should be applied to close the luminal defect.

Recurrence rates remain a challenge for piecemeal resections of polyps. A systematic review and meta-analysis of 33 studies found the recurrence rate after piecemeal and en bloc resections to be 20% and 3% (26). Over 90% of recurrences occurred within 6 months leading the authors to recommend follow-up colonoscopy at 6 months.

Endoscopic submucosal dissection (ESD)

ESD was originally developed in Japan in the early 20th century for the treatment of low risk gastric cancer (27). ESD indications now include colorectal lesions greater than 20 mm that were traditionally removed piecemeal (28). The goal of ESD is to remove lateral spreading tumors/

lesions en bloc to decrease recurrence. ESD provides a curative option with en bloc resection of low risk submucosal invasive cancer (defined as well- or moderately differentiated adenocarcinoma with submucosal invasion $\leq 1,000$ μm that cannot be accomplished by EMR) (29). Identifying appropriate lesions for ESD led to the development of the Kudo, Paris, and NICE classification systems to assess the level of submucosal invasion (30–32).

Similar to EMR, ESD starts with a submucosal injection that contains pigmentation to lift and mark the mucosal layer, followed by circumferential marking of the lesion with a needle knife that is connected to electrocautery (33,34). A plastic cap is attached to the tip of the colonoscope to help retract the lesion off of the base and provide hemostasis. The dissection is performed at the submucosal plane just above the muscularis propria to prevent deep thermal injury and perforation. Change in patient position can sometimes provide traction by gravity to pull the flap of tissue away during dissection and provide a better view of the submucosal plane (33).

A meta-analysis including 8 studies with over 2,000 lesions compared EMR and ESD and their rates of en bloc resection, curative resection, recurrence, and adverse events [Figure 1 (35)]. It was worth noting that these studies consisted of historical cohort and case-control studies, with no randomized controlled trials. The authors concluded that ESD has a higher rate of en bloc and curative resection with a lower recurrence rate than EMR (91.7% vs. 46.7%, 80.3% vs. 42.3%, and 0.9% vs. 12.2%), but is more likely to result in perforation (5.7% vs. 1.4%) and takes 3 times longer even in experienced hands (35). The rates of delayed bleeding are similar between ESD and EMR (3.5% vs. 2%).

ESD is a technically challenging and time-consuming procedure. The higher prevalence and screening of gastric cancer in Japan allows endoscopists to first master this technique in the distal stomach, where early neoplasms are most commonly found. Gastric anatomy makes it easier to perform endoscopic interventions as compared to the angulations and folds in the colon where the endoscope is more difficult to maneuver and the muscle layer is thin (18,36). In the Western world where gastric cancer incidence is much lower, endoscopists lack the opportunity to perfect the techniques of ESD in easier locations prior to graduating to more challenging ones in the colon (27,29). For endoscopists with experience in gastric ESD, the learning curve for colon ESD ranges from 30–50 cases (37,38). For endoscopists in the United States without experience in gastric ESD using an un-tutored prevalence

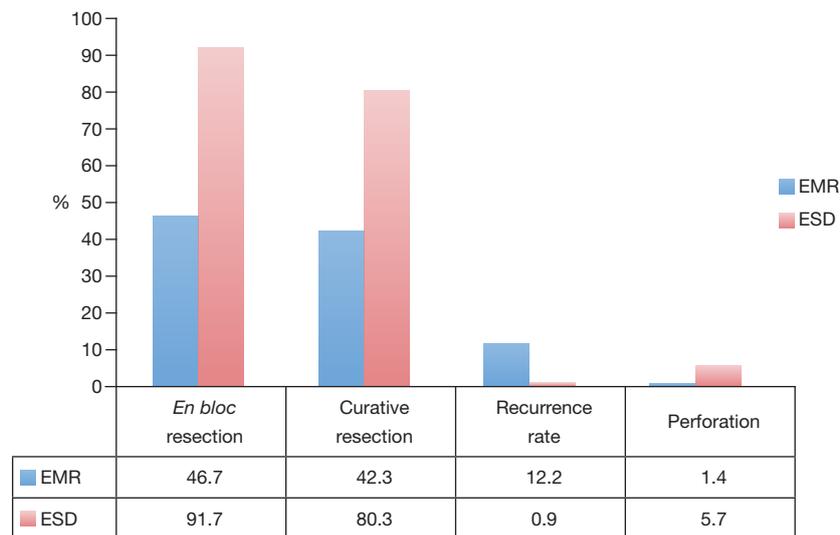


Figure 1 Meta-analysis of 8 studies comparing EMR and ESD (35). EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

based approach the number of cases needed to be proficient is estimated to be 250 (39).

Fuccio *et al.* recommend ESD be used specifically for lesions that are highly suspicious for submucosal invasive cancers involving only Sm1 and EMR be employed for all other lateral spreading lesions (40). Their meta-analysis of 11,260 ESDs identified submucosal invasive cancers involving Sm1 in 8% of the lesions while deeper lesions were seen in 7.7% of specimens. Standard of care for patients with lesions greater than Sm1 is surgical resection. The authors estimated that 16.7 ESDs would need to be performed to prevent one surgery.

Combined laparoscopic and endoscopic resections (CLERs)

CLERs are described for difficult polyps that are not amenable to standard approaches, such as EMR or ESD. CLER encompasses a spectrum of procedures employing both laparoscopic and endoscopic techniques to improve visualization of the difficult polyp, and thus the safety and precision of the procedure. CLER offers the advantage of the ability to fully mobilize the colon laparoscopically and guide the colonoscope under direct visualization. The following table reviews single center studies with at least 30 patients demonstrating success rates from 74–96% (41) (Table 1). Length of stay is 1–2 days and recurrence rates are low. Patient selection and endoscopist/surgeon experience is essential to the successful completion of these novel

procedures.

Surveillance after polypectomy

The current recommendations for surveillance colonoscopy after successful polypectomy are based on risk stratification. According to the 2012 US Multi-Society Task Force Update patients with low risk, defined as one or two small tubular adenomas, should undergo surveillance at a 5–10-year interval. Patients with high risk polyps, defined as adenoma ≥ 1 cm, high grade dysplasia, or villous histology, should undergo surveillance in 3 years (47). There is no clear evidence to support when to perform surveillance in patients who have undergone piecemeal polypectomy for laterally spreading tumors despite their significant recurrence rate.

Malignant polyps

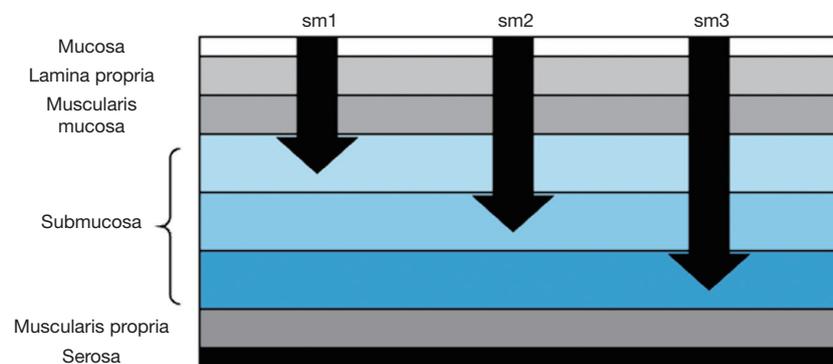
Malignant polyps comprise 12% of resected polyps (48). It is essential for endoscopists to identify features of malignant polyps at the time of the index colonoscopy and manage them appropriately by marking the polypectomy site, resecting them in entirety instead of piecemeal, and referring the patient for surgical evaluation.

Differentiating between superficial (< 1 mm) and deep (> 1 mm) submucosal invasion is essential for management (endoscopy or surgery) of malignant polyps. Two commonly available techniques to identify submucosal

Table 1 Combined laparoscopic and endoscopic resections of colorectal polyps with at least 30 patients

First author, year	Number of patients	Success rate (%)	Median size (cm)	Time (minutes)	Length of stay (days)	Recurrence N, follow-up in months
Franklin, 2007 (42)	110	83	2.3	NS	1	NS
Wilhelm, 2009 (43)	146	82	NS	92	8	1, 31 months
Goh, 2014 (44)	30	73	1.4	105	2	0, 20 months
Lee, 2013 (45)	65	74	3.0	145	1	5, 65 months
Crawford, 2015 (46)	30	96	4.0	71.5	2	1, 22 months

NS, not-specified.

**Figure 2** Colon wall anatomy.

invasion are narrow band imaging (NBI) and magnifying chromoendoscopy (M-CE). Systematic review and meta-analysis including 17 studies determined the sensitivity and specificity of NBI and M-CE as 74% and 84% and 98% and 97%, respectively (48). If a polyp is too large to safely remove or has deep submucosal invasion, the lesion should be marked and the patient referred for surgical resection.

Many times malignancy is discovered when the pathology results come back. In these cases, multiple factors determine management: morphology, depth of invasion, margins, and histology (49). Morphology and depth of invasion are closely linked with the definitions of invasion and associated risk is dependent on whether the polyp is sessile or pedunculated. For sessile polyps, removed en bloc, the depth of submucosal invasion (Sm1-invasion into the upper third, Sm2-invasion into the middle third, Sm3-invasion in the lower third) determines the risk of lymph node metastases [Figure 2 (50,51)]. Invasion into the lower third of the submucosa (Sm3) is associated with a 23% rate of lymph node metastases (52).

For pedunculated polyps, removed en bloc, Haggitt

levels 1–4 are used for depth of invasion. Level 1 indicates invasion of the submucosa confined to the head of the polyp, level 2 is submucosal invasion in the neck of the polyp, level 3 is submucosal invasion in the stalk, and level 4 is submucosal invasion at the base of the polyp (53). Level 4 invasion is associated with a 27% rate of lymph node metastases (54).

Margins are determined ideally in pedunculated or sessile polyps removed en bloc. Piecemeal resection makes margin determinations unreliable. For en bloc polyp resections, margins of at least 2 mm are recommended (55,56). Malignant polyp features that mandate surgical resection with appropriate segmental colectomy are lymphovascular invasion, poor differentiation, piecemeal excision, submucosal invasion >1 mm, and margins less than 1 mm (2 mm used as well) (57,58). Tumor budding, defined as a single cell or cluster of tumor cells not exceeding four, has been added by the College of American Pathologists to their colon cancer protocol (59). Tumor budding is associated with increased risk for lymph node metastasis and is included as an adverse risk factor in the National

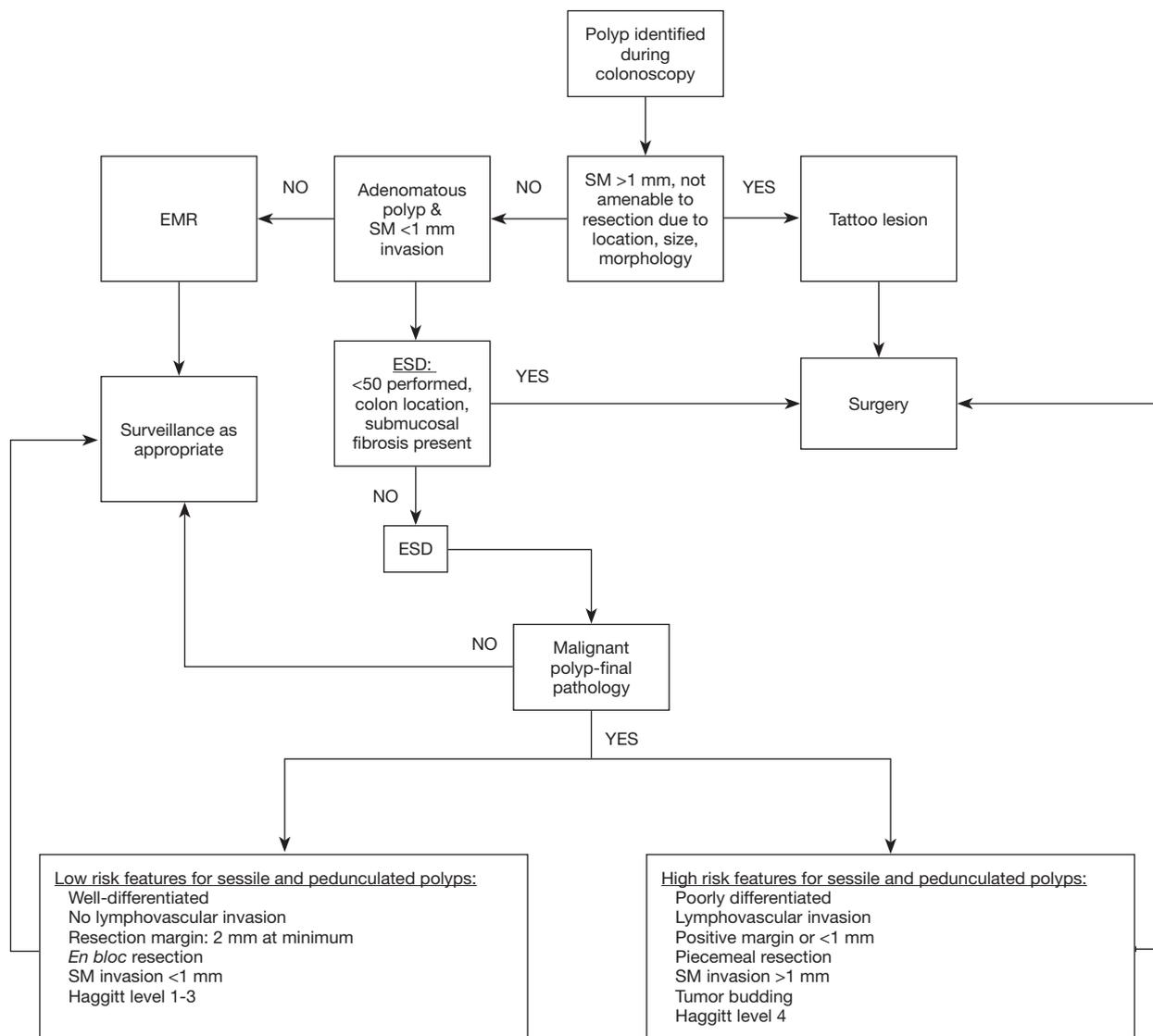


Figure 3 Advanced polyp pathway. SM, submucosal.

Comprehensive Cancer Network 2019 guidelines for colon and rectal cancers (59-63).

Conclusions

Endoscopic polypectomy is an important therapeutic option in the treatment of colorectal polyps. Different techniques are currently described in the literature: forceps, snare, EMR, and ESD. Endoscopists should be familiar with each technique and complication profile in determining which one to offer based on patient and lesion characteristics as well as their own skill set. Future studies are necessary

in comparing the safety and efficacy of some of the novel techniques such as ESD.

Please see Figure 3 for advanced polyp pathway.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Jeffrey M. Marks and Ryan M. Juza)

for the series “Surgical Endoscopy: Essential Skills in Gastrointestinal Surgery” published in *Annals of Laparoscopic and Endoscopic Surgery*. The article has undergone external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/ales.2019.08.09>). The series “Surgical Endoscopy: Essential Skills in Gastrointestinal Surgery” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/ales.2019.08.09

Cite this article as: Lam W, Times M. Colonoscopic polypectomy. *Ann Laparosc Endosc Surg* 2019;4:97.