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INVITED REVIEW

Endoluminal Surgery: Where are We Headed?

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ABSTRACT

The expansion of colorectal cancer screening programs predicts a remarkable increase in non-malignant polyps and early-stage colorectal neoplasia. While the majority of these polyps are managed endoscopically, a large number of patients are referred to surgery. Over thirty thousand patients with large colon polyps undergo surgical procedures, such as colectomy or proctectomy, in a given year in the United States of America. Such surgeries lead to organ loss due to benign disease and have significant morbidity and mortality rates. Conversely, endoluminal surgery (ELS) may provide organ preservation with low morbidity and mortality for the majority of these patients. In this review, we aimed to discuss ELS and future directions in this field.

Keywords: Endoluminal surgery, advanced endoscopy, endoscopic submucosal dissection, endorobotic submucosal dissection

Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer death in the United States.[1] Colonoscopy and polypectomy starting at the age of 45 years old is well established in the United States as a screening program and has decreased CRC-related mortality.[2] While most polyps detected during routine colonoscopy are less than 10 mm in size and are treated with simple techniques, such as cold forceps or snaring, advanced endoscopic treatment options can be offered for larger polyps with advanced morphological features that are not amenable to conventional endoscopic removal.[3]

Surgery for non-malignant polyps and CRC has been increasing in the last decade, and 25% of all colorectal resections are performed for non-malignant polyps with a significant annual increase from 5.9 in 2000 to 9.4 in 2014 per 100,000 adults.[4] The performed colectomies have 0.8% in-hospital mortality and 25% morbidity within 30 days of surgery.[5] Surgeons considering surgery for non-malignant polyps should be aware of this potential for morbidity and mortality. Furthermore, in 92% of these resections the final pathology after organ resections does not identify invasive cancer.[6]

Advanced endoscopy techniques had been developed and are well described to treat large colorectal lesions and achieve organ preservation. These were first described in Japan and have gradually become more prevalent all over the world. The procedures were first described for upper gastrointestinal system (GI) lesions and then adapted to the lower GI tract. The significant difference in the anatomy of the lower GI compared to the upper GI and the technically demanding procedures with a long learning curve limited the widespread use of advanced endoscopy in the colon and rectum. Advanced endoscopy has recently increased interest due to its technical advantages and proposed organ preservation despite these limitations.

Advanced endoscopy techniques and the development of endoluminal surgery (ELS) is a rapidly progressing field in the treatment of lower GI lesions. ELS offers organ preservation with less invasive methods compared to surgery and can even be performed in outpatient settings.

Indications for Endoluminal Surgery

Current guidelines recommend resection of all mucosal lesions, reserving advanced endoscopy techniques for larger lesions.[3,7] Endoscopic Mucosal Resection (EMR) is defined as a technique involving submucosal injection and snaring of the lesion. In contrast, Endoscopic Submucosal Dissection (ESD) is defined as submucosal injection followed by mucosal incision and submucosal dissection with a needle-type knife

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and complete removal of the lesion in one piece. Precutting EMR is the term used for a technique where snaring is performed without dissecting the submucosal layer after incising the lesion's circumference. If the submucosal layer is dissected and additional snaring is performed to complete the resection of the lesion, the procedure can be defined as hybrid ESD.

The primary aim of polypectomy is the complete removal of the colorectal lesion. Based on current scientific evidence, endoscopists should employ the most favorable, complete, safest, and efficient technique with the most negligible recurrence probability. EMR is a more common technique performed for smaller lesions, whereas ESD is reserved for larger lesions. Compared to EMR, ESD was found to have higher en-bloc resection and lower recurrence rates with comparable complication rates.[8,9] In addition, an en-bloc resection yields increased accuracy on histopathologic evaluation and decreased risk for further surgical interventions.[10]

Preprocedural Management

Endoscopists should evaluate colored images of the previous colonoscopy reports and pathology reports. Such evaluation provides an opportunity to predict planned intervention and additional equipment needed during the procedure. Patients' medical histories and medication use should be questioned in detail. Information about anticoagulant use and dosage is crucial. The anticoagulants are typically stopped 2-7 days prior to the procedure. The decision whether a procedure will be performed in an endoscopy suite or in the operating room is currently made by reviewing all the available data and taking into account patient specific risk factors (Figure 1). Operating room settings may be preferred for patients who have comorbidities and/or high-risk lesions, as well as for planned combined endolaparoscopic (CELS) procedures. The operating room is also recommended if additional endoluminal enabling platforms are planned to be used.

The endoscopists can use advanced endoscopic imaging techniques, such as narrow-band imaging[11] and focal interrogation, Paris classification[12], and Kudo pit pattern[13] to predict the risk of submucosal invasion. Where available, these methods are helpful to evaluate the surface morphology related to submucosal invasion risk. Perioperative evaluation of patients is critical for successful results.

Submucosal Injection

Injection of lifting solution into the submucosal space is the first important step in advanced endoluminal procedures. Common submucosal lifting agents are saline, hyaluronic acid, glycerol, dilute albumin, and brand-name gels. The submucosal saline injection will suffice and provides a lift that lasts approximately three minutes for simple polypectomies. However, advanced endoluminal procedure typically takes longer. ORISE™ Gel Submucosal Lifting Agent (Boston Scientific) and Eleview® are Food and Drug Administration-approved and readily available lifting agents on the market.[9] The pre-prepared form with no need for mixing before the injection facilitates the procedure time by shortening the duration of the preparation step. In addition, longer-lasting solutions in the submucosal space should be preferred to reduce the time loss due to repetitive injections. Thus, saline is not a preferred injectate as its stay in tissue is limited, and it disperses quickly.[14] In addition to these solutions, diluted adrenalin (1 mL of 0.1% adrenalin) and hydroxyethyl starch solution mixed with methylene blue or other dyes can be used.[15]

The injection step aims to achieve an adequate lift of the lesion. The injection needle should be advanced tangentially along the mucosa (Figure 1). If tissue elevation is not observed after starting the injection, this could be due to entry into an incorrect plane, typically into the abdominal cavity. The injection needle should be adjusted slightly

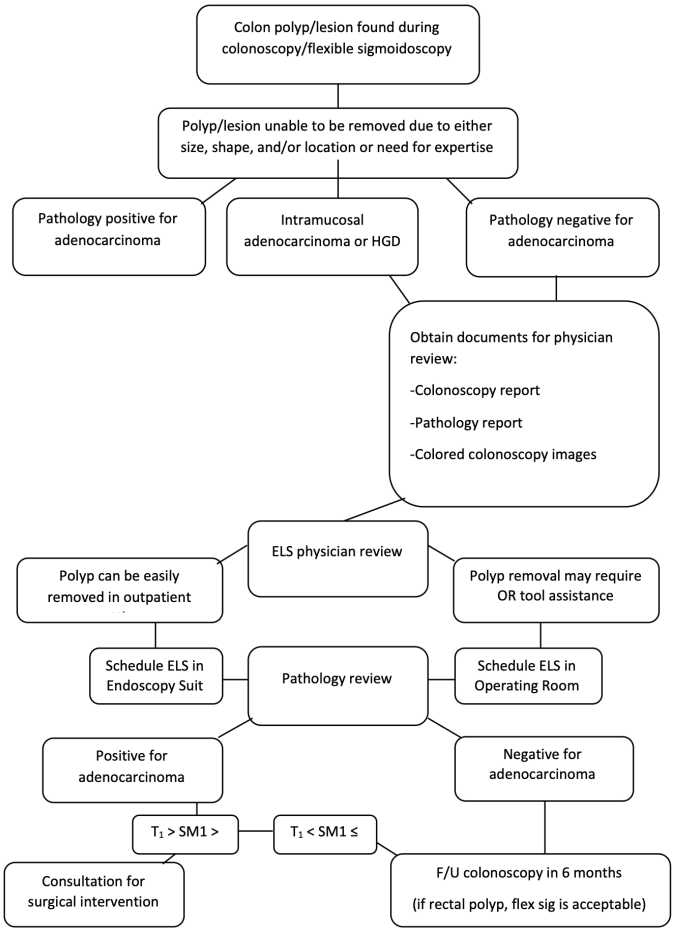

Figure 1. Current ELS Care Path in the management of complex colorectal lesions designed by the Endoluminal Surgery Center, Cleveland Clinic, Ohio, United States of America
ELS: Endoluminal surgery

and realigned before continuing the injection. For lesions located on a fold, it is advantageous to start the injection along the far aspect (oral/proximal side) of the lesion to lift the lesion towards the operative field of view. The lesion may fall away from the view if the injection is started from the distal (anal) side. Despite ensuring the correct plane is injected, there may be no obvious or adequate lift (non-lifting sign). This sign could be due either to deep invasion or fibrosis arising from previous interventions to the lesion. Endoscopists should stop the procedure in case of suspicion of deep invasion.

Endoscopic Mucosal Resection

EMR consists of snaring the lesion after the injection step. The goal should be en-bloc lesion removal, but repeating the snaring as few times as possible is favored when not practical. Increasing the number of pieces snared will decrease the adequacy of the histopathological examination. There are many different shapes and sizes of snares available. The endoscopists should choose the appropriate snare shape and size for the lesion. At least 2-3 mm normal mucosal margin should be targeted while snaring. Although not encouraged, if the resection will be piecemeal, the snare should be aligned at the resected margin edge and be repeated until complete lesion removal.

Endoscopic Submucosal Dissection

ESD applies surgical principles, that is en-bloc resections with clear margins. The dissection is performed with either endoscopic knives or snare tips. There are different knives available, including the FlexKnife Electrosurgical Knife (Olympus, Tokyo, Japan), HookKnife™ (Olympus America Inc., Center Valley, PA, USA), the DualKnife™ (Olympus America Inc., Center Valley, PA, USA), the HybridKnife® (ERBE, Tübingen, Germany) and more recently the ORISE™ ProKnife (Boston Scientific, Marlborough, MA, USA). The combined knives integrate the injection needle and knife functions into one instrument and can decrease the procedure time lost during device placement for each step. The decision about which instrument to use should be based on the availability of the device and the endoscopist's comfort level with it.

Precut EMR and Hybrid ESD

Occasionally, a hybrid method comprising a combination of EMR and ESD can be helpful and time-efficient when pure ESD is not achievable. ESD techniques can be used to define the resection borders, perform the lift, and get the dissection started. Afterward, the remaining central or peripheral resection can be performed with a large snare. The submucosal plane should be visualized clearly during this step, and in case of elevation loss, injections should be repeated as necessary. These steps should be continued until complete resection is achieved. It is essential to clean the field after dissection, visualize the resected area, inspect for any remaining island-like remnants of the lesion, and identify any injury or full-thickness defects. If any submucosal defects are observed, they should be closed with endoscopic hemoclips. Multiple clips can be applied for closure of the defect if necessary.

Novel Endoluminal Platforms

Although ESD offers a way to avoid unnecessary surgery and provides better results compared to piecemeal resections, it is not widely applicable and adapted due to technical challenges including poor stabilization and visualization. Additionally, the required technical skills are very hard to acquire with a steep learning curve. New endoluminal devices are being developed to facilitate the process and increase procedural success rates. They aim to help the endoscopist stabilize the procedure field and incorporate surgical principles, such as traction-counter traction.

ORISE Tissue Retractor System (ORISE TRS; Boston Scientific, Marlborough, MA, USA) consists of a cage-like structure with two instrument channels and can be inserted over a standard colonoscope. This platform stabilizes the intraluminal space, and endoscopic instruments can be introduced to retract the lesion. After starting the dissection, this platform can be introduced with the colonoscope, positioned on the lesion, and the cage-like structure is then opened. Like other platforms, this provides stability of the dissection field, and separate instrument channels allow forceps to be introduced for precise and active real-time retraction.

DiLumen C^{2}™ Endolumenal Interventional Platform is a novel endoscopic stabilization and tissue manipulation device facilitating traction and en-bloc complete removal of complex colorectal lesions. The DiLumen platform consists of a soft, flexible sheath that fits over standard and small-diameter endoscopes. The device employs two balloons, one behind the bending section of the endoscope and the second in front of the tip. When both balloons are deployed and inflated, the area in between is stabilized. In addition, the platform employs two 6 mm working channels at the 3 and 9 o'clock position of the endoscope for graspers and scissors. These instruments can be used for retraction and cutting.

Endorobotic Submucosal Disection

The DaVinci Single Port robotic platform can be used to perform rectal submucosal dissections (Figure 2). This platform is a semi-flexible robot that can reach up to 20-25 cm from the anal verge. We have performed more than ten submucosal dissections in the rectum with the platform.

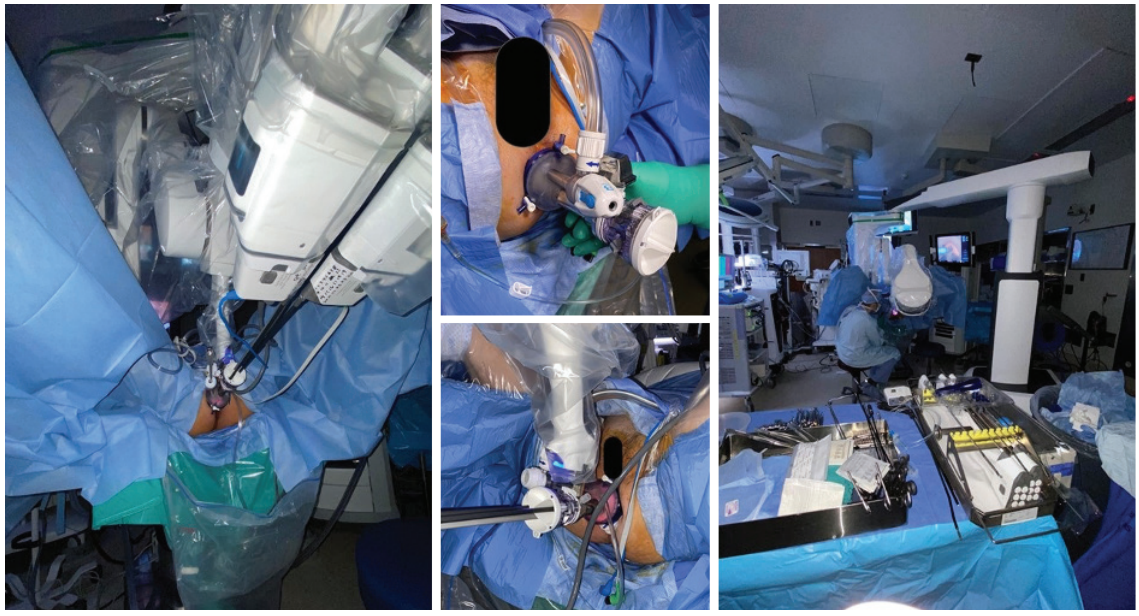

Figure 2. Single port robot (SP DaVinci Robot) and use of Endorobotics

With the development of novel, fully flexible, robot-assisted surgical systems, there may soon be significant progress in the current understanding of ELS. These platforms might enable surgeons to perform incisionless surgeries through the gastrointestinal wall, that previously could only be performed via transabdominal surgery.

However, the identification of specific biomarkers that detect genetic aneuploidy/instability will further help in assessing the invasiveness of the tumor, level of invasiveness, and even detecting metastatic lymph nodes. More accurate preoperative or intraoperative evaluation may enable resection of just the tumor and involved lymph nodes or surveillance.

Surveillance

After ELS every patient should undergo periodic follow-up colonoscopy (sigmoidoscopy is acceptable for rectal lesions). This follow-up colonoscopy aims to detect local recurrence and/or metachronous lesions. There is no consensus on the timing of surveillance after mucosal resection, but it is generally accepted that follow-up colonoscopy should be performed depending on individual pathology results and quality of the specimen with proximity to en-bloc resection technique. In addition, individual risk factors play a role: for more than one lesion or carcinoma and accompanying comorbidities should be considered when proposing the frequency of surveillance. Eastern and Western guidelines propose different periods but, in general, follow-up endoscopy is recommended on the sixth month after the index procedure.[7,16,17] Subsequent colonoscopies after this first follow-up are recommended to occur at the first and third year, in case of no recurrence.

Conclusion

ELS is a promising, minimally invasive approach for organ preservation for the GI tract and a potential major advance for GI surgery. Endoscopists may overcome the challenges of advanced endoscopic tissue resections with the help of new instruments and platforms where traction and counter-tractions can be applied intraluminally. These procedures can be assisted with CELS surgery. Thus surgeons can quickly and naturally adapt these endoluminal techniques. Although ELS is considered challenging, it will continue to progress and potentially gain popularity in the near future. Increased education, research, and availability of the tools to perform these procedures will help more surgeon endoscopists become adept over time. As ELS means there is less need for intra-abdominal surgery, ELS could be the next big step for minimally invasive surgery. Fully flexible endorobotic platforms with stable camera positioning, increased dexterity, and precision will become a reality and this will push the field of ELS forward.

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