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## Endoscopic resection of tumors in the lower digestive tract

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the endoscopic resection of gastrointestinal tract polyps has become a widely used treatment. Colorectal polyps are the most common type of polyp, which are best managed by early resection before the polyp undergoes malignant transformation. Methods for treating colorectal tumors are numerous, including argon plasma coagulation, endoscopic mucosal resection, endoscopic submucosal dissection, and laparoscopic-endoscopic cooperative surgery. In this review, we will highlight several currently used clinical endoscopic resection methods and how they are selected based on the characteristics of the targeted tumor. Specifically, we will focus on laparoscopic-endoscopic cooperative surgery.

**Key words:** Colorectal tumor; Endoscopic resection

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**Core tip:** The best case scenario for patients with lower digestive tract tumors is to detect and resect the tumor before it undergoes malignant transformation. However, modern technologies for tumor resection are numerous and there may be specific indications for the implementation of one technology over another. Therefore, we will discuss the current clinical endoscopic resection methods and the process for selecting specific interventions. We wish to highlight laparoscopic-endoscopic cooperative surgery, because it may be of assistance in endoscopic treatment and could remarkably decrease the rate of later surgical repair.

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## Abstract

As endoscopic technology has developed and matured,

## INTRODUCTION

Colorectal tumors are common in modern society and

although numerous new technologies have become available to locate, identify, and treat these tumors, early detection and removal (*e.g.*, during the polyp stage before malignant transformation) are still the key to long term survival and a favorable overall prognosis<sup>[1,2]</sup>. As a result, endoscopic methods have steadily developed to better meet these requirements. A study by Winawer *et al.*<sup>[3]</sup> showed that endoscopic removal of colorectal adenomas can reduce the incidence rate of colorectal cancer by about 76%-90%. The current clinical endoscopic polypectomy methods are numerous and varied. Through careful observation of the distribution, size, morphology, and pathological features of colorectal polyps, clinicians/endoscopists can select the appropriate endoscopic resection treatment to avoid repeated unsuccessful procedures and improve the quality of life of the patient<sup>[2]</sup>.

## ENDOSCOPIC DIAGNOSIS BEFORE RESECTION

Before endoscopic resection, a comprehensive evaluation of the lesion is required. Ordinary endoscopy, magnifying endoscopy, or narrow-banding imaging (NBI) can be used to make a preliminary observation<sup>[4]</sup>. If the pathology confirms that the lesion is an adenoma, endoscopic resection can be performed. Pedunculated adenomas can be removed easily by endoscopic resection, regardless of the size of tumor; if the adenoma is sessile, the resection will be based on relevant patient parameters (age, body condition, and the patient's wishes)<sup>[5]</sup>. If pathological examination shows that the lesion is malignant, a "lifting sign" should be judged by injecting normal saline and indigo dye at the basal submucosal layer of the lesion. If the "lifting sign" is negative, the tumor has invaded and extended into the submucosa or even below<sup>[6]</sup>. Research has confirmed that for lesions confined to the mucosal layer, lymph node metastasis generally does not occur. Tumors that extend deeper into the submucosal layer can be divided into categories SM1-SM3. SM1 tumors (submucosal invasion < 1000  $\mu\text{m}$ ) have a low risk of lymph node metastasis, while the SM2 and SM3 tumors (submucosal invasion more than 1000  $\mu\text{m}$ ) have a higher lymphatic metastasis risk-up to 12.5%<sup>[7-9]</sup>. Tumors with a negative "lifting sign" should be surgically removed, rather than removed endoscopically.

## ENDOSCOPIC RESECTION METHODS

### *Argon plasma coagulation*

The principle of argon plasma coagulation (APC) is to use a specialized device to deliver ionization energy from argon; this high frequency energy can be implemented to solidify the tissue surface. Presently, APC plays an important role in maintaining hemostasis and cauterizing lesions during surgical and endoscopic

procedures taking place in the human gastrointestinal tract<sup>[10]</sup>. The advantages of APC for treating colorectal lesions are that it is a rapid and efficient procedure that produces only a small vulnus and is generally well-tolerated by patients<sup>[11]</sup>. Some studies show that the most outstanding advantage of APC is its self-limited solidification depth. The damage of solidification generally does not extend more than 3 mm, minimizing the risk of perforation<sup>[12]</sup>. Based on the characteristics of the laser and the high frequency electric knife, APC can effectively be used to stop bleeding during a gastrointestinal procedure. Furthermore, during the operation, the probe does not need to contact the tissue, reducing the risk for adhesions or hemorrhages<sup>[13]</sup>. However, APC does have some limitations. Mainly, it is difficult to obtain pathological specimens with this technique, making it nearly impossible to determine the invasion depth, such that the cutting edge of the polyps is unclear.

### *Endoscopic mucosal resection*

Endoscopic mucosal resection (EMR) has become a routine method for the treatment of early gastrointestinal mucosal lesions<sup>[14]</sup>. The general method of EMR is adapted to the submucosal injection of liquid saline to separate the lesions from the underlying muscle layer, after which lesions can be completely removed with a snare. The method is simple, safe, produces a small vulnus, is easily adaptable, and fairly easier to master, even for less experienced endoscopists<sup>[15,16]</sup>. However, there is the risk for rare and serious complications, such as intestinal perforation and bleeding, although these can be remedied by endoscopy or surgery. The incidence of perforation is very low (0.7%-1.3%), and the risk for bleeding is also fairly low (5.0%-8.1%)<sup>[17,18]</sup>. Some studies show that effective/optimized submucosal injection can help to prevent complications and ensure the safety of EMR<sup>[19]</sup>. Compared to APC, EMR has some advantages. Namely, EMR allows for pathological examination of the lesion after EMR to determine invasion depth and the cutting edge. However, due to the likelihood for electrocoagulation through snaring, EMR is only suitable for the complete resection of tumors with diameters that are less than 20 mm. Here, the complete resection rate is 64.3%-77.4%, and the recurrence rate is very low (0%-3.6%)<sup>[20,21]</sup>. If the tumor is larger than 20 mm, the complete resection rate drops significantly to 48.1%-32.9%, while the recurrence increases to 16%-25.7%<sup>[22,23]</sup>. Therefore, EMR is not an appropriate choice for the treatment of particularly large (greater than 20 mm) gastrointestinal tumors.

### *Endoscopic submucosal dissection*

Endoscopic submucosal dissection (ESD) was developed based on EMR techniques and was named after it was approved as a new resection method in 2003. In this procedure, an insulation tipped knife (knife IT) is

instrumental for performing ESD. Compared to EMR, ESD can not only provide complete specimens for more reliable pathological examination, but it can also be used to fully resect the tumor with a low rate of recurrence<sup>[24]</sup>. For tumors less than 20 mm, the complete resection rate is 82.6%-97.7% and the recurrence rate is nearly 0%<sup>[21,25,26]</sup>. However, if the tumor is larger than 20 mm, the complete resection rate drops a little to 74%-91.8%, but the recurrence rate remains 0%-1%<sup>[17,22,23,25]</sup>. During the ESD procedure, the operator should pay attention to the "lifting sign" after submucosal injection, which can be used to determine the lesion depth. If the lesion is located in the mucous layer with a proper boundary to the muscularis propria and has a positive "lifting sign," it can be removed by ESD<sup>[27,28]</sup>. However, the rate of perforation in ESD is higher than that for EMR, because the submucosal layer is nearer to the muscularis. For this procedure, which is more complicated than EMR, the incidence of complications also correlates with the operator's technical proficiency<sup>[29]</sup>. Nonetheless, in some studies, the bleeding rate of ESD remains low (0.4%-2.5%), although the risk of perforation is slightly higher (2.9%-5.3%)<sup>[30,31]</sup>.

#### **Laparoscopic-endoscopic cooperative surgery**

At present, endoscopic therapy is not only applied to resecting colorectal polyps, but also to the treatment of early colorectal cancers that are located in the mucosal layer. Through endoscopic resection, patients can avoid laparotomy, sustain lesser injury, and recover quickly<sup>[32]</sup>. However, the colonoscopy field of vision is limited in the intestinal lumen, such that the condition of the bowel wall or abdominal cavity is unclear. Some lesions located in the splenic or hepatic flexure can make endoscopic resection difficult. Laparoscopic-endoscopic cooperative surgery (LECS) takes advantage of characteristics of both laparoscopic and colonoscopic procedures. LECS is often implemented when the lesion is difficult to be removed or cannot be completely resected by endoscopic methods alone<sup>[33]</sup>. Under the guide of a colonoscope, the laparoscope can look for and identify the intestinal site where the lesion is located and dissociate it from this site if necessary. By pulling and pushing the laparoscope upward, the lesion may be exposed so that endoscopists can use EMR or ESD to remove the lesion. During this process, the operator can focus on the complete excision of the lesion and does not need to be concerned with possibility of perforation. If perforation or bleeding occurs, laparoscopy can be used to repair the perforation and return to hemostasis immediately. However, no randomized controlled trials have been performed to evaluate LECS in the treatment of lower digestive tract tumors. Nonetheless, select published LECS cases suggest that it is a feasible procedure for the *en bloc* resection of some colonic lateral spreading tumors that would be otherwise difficult to resect using exclusively endoscopic methods<sup>[34-36]</sup>.

## **CHOOSING THE ENDOSCOPIC TREATMENT**

### ***Tumors with a diameter less than 3 mm***

For small tumors less than 3 mm in diameter, APC can be used for solidification of the lesion. However, as this technique cannot be used to collect pathological specimens, long-term endoscopic follow-up is required<sup>[37]</sup>.

### ***Tumors with a diameter less than 20 mm***

For lesions in this size category, according to a study by Lee *et al.*<sup>[26]</sup>, there are no significant differences in the complete resection rate between EMR (82.6%) and ESD (64.3%) techniques. Although EMR has a recurrence rate of 3.6%, the risk of cancer progression for small tumors is minimal and the main pathological type for this size tumor is adenoma; therefore, EMR is suitable for the removal of small lesions and is a fairly easy technique to master, even for less experienced endoscopists. The risk of perforation with EMR is lower than that with ESD, and it is regarded as a quicker and safer choice for lesions with a relatively smooth surface without signs of bleeding and erosion<sup>[18,38]</sup>. However, there are some exceptions. If the endoscopic diagnosis (NBI or magnifying endoscope) strongly indicates that the lesion is malignant and the pathological examination shows the same results, the tumor must be excised by ESD and the patients should undergo close follow-up in the future.

### ***Tumors with a diameter more than 20 mm***

Some studies report that the proportion of adenocarcinomas significantly increases in tumors larger than 20 mm in diameter, since the degree of tumor malignancy is often associated with the relative tumor size<sup>[39]</sup>. Other studies report that the size of the tumor can be at least partly used as an index to predict the degree of malignancy. The possibility of recurrence for tumors greater than 10 mm diameter is relatively high<sup>[26]</sup>. Early adenocarcinomas have characteristics of invasion, recurrence, and metastasis, and due to a lower complete resection rate and high recurrence rate, EMR is not suitable for these kinds of tumors. Fortunately, ESD can be used to remove larger tumors with much higher complete resection rates and lower recurrence rates. However, ESD still has some limitations, especially for larger laterally spreading tumors. Here the excised area is often too large, translating to an extremely high risk of perforation<sup>[40]</sup>. Once a perforation occurs, a surgical repair or intestinal resection is needed to repair the large defect left by ESD. Therefore, LECS may be a better choice to ensure a complete resection, while minimizing the risk of serious complications. Based on the assistance of a laparoscope, the visibility of lesion is greatly enhanced and the operator can focus on the complete excision of the lesion while not worrying about the possibility of perforation, which can easily

and rapidly be repaired using the laparoscope to stitch the perforated area. Rapid detection and repair of any perforations greatly reduce the risk of abdominal infection. Therefore, in certain situations, LECS can not only be minimally invasive, but also offers better and safer therapeutic effects<sup>[41,42]</sup>.

## CONCLUSION

Endoscopic resection presents a great technological leap in the diagnosis and treatment of colorectal tumors, as well as an important preventive measure to remove polyps in their premalignant stages. In recent years, some new technologies, such as magnifying endoscopy and NBI have improved the detection rate of early colorectal cancers, which improves long term survival and the resulting quality of life. At the same time, with the continuous development of endoscopic treatment equipment and the introduction of new technologies, most colorectal polyps and early cancers can now be resected by minimally invasive EMR, ESD, or LECS techniques, which can now achieve the same effects as surgery. However, when endoscopic treatment is to be used, the indications should be carefully considered following evaluation of the relevant patient and pathological parameters, along with the likelihood of complete resection and risk for complications. Therefore, initial colonoscopy examination is crucial. Although minimally invasive and often successful in full resection, endoscopic resections do have some limitations. If the cancer invades deep into the submucosal layer, belongs to the lower differentiation, or contains a lymphatic or venous tumor thrombus, additional radical surgical operation will still be required.

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