Endoluminal Therapy in Colorectal Cancer

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Abstract

Keywords

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Appropriate endoscopic resection for colorectal polyps can present a challenge to endoscopists, as these lesions may harbor malignancy. With recent advances in endoscopy, however, we are now entering an exciting frontier of endoscopic therapy for gastrointestinal lesions. These techniques include endoluminal mucosal resection and endoscopic submucosal dissection, which may be utilized on several colonic lesions. This article will discuss these principle endoscopic techniques, their outcomes, and briefly highlight their influence on endoscopic interventions, including transanal endoscopic microsurgery and natural orifice transluminal endoscopic surgery.

Endoscopy is a diagnostic and therapeutic tool for gastrointestinal tumors. Multiple studies, primarily in Japan, have identified its use in esophageal, gastric, and lower gastrointestinal tumors.¹ The techniques originally designed for treatment of gastric and esophageal lesions have been pioneered in lower gastrointestinal polyps. These techniques include endoluminal mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Surgeons now have alternatives to operative treatment of lower gastrointestinal lesions that allow full thickness resections which carry a higher mortality and morbidity than simple endoscopic resection.² The purpose of this article is to describe these endoscopic interventions and their utility in specific lower gastrointestinal polyps, with a brief highlight on transanal endoscopic microscopic surgery (TEM), and the future of natural orifice transluminal endoscopic surgery (NOTES).

Lower Gastrointestinal Polyps

To adequately determine endoscopic resection candidates, one must first be knowledgeable about lower gastrointestinal lesions. Generally, lower gastrointestinal lesions can be grossly characterized as polypoid or nonpolypoid. Polypoid lesions, with or without a stalk, are easy to excise completely, using either hot or cold snare polypectomy,³ and carry a smaller malignancy rate than nonpolypoid lesions.^{4,5} Nonpolypoid lesions are further classified into sessile lesions (where the height is greater than width), depressed lesions (flat lesions

with depressed centers), flat lesions (less than 10 mm circumference), and lateral spreading lesions (greater than 10 mm circumference).⁶ These lesions carry an increasing malignancy rate, respectively.⁶

Endoscopically, these lesions are identified based on their gross appearance: size, color change, firmness, interruption of the capillary network, deformation of the colonic wall, spontaneous bleeding, lesion shape, changes with air inflation and deflation, and interruption of innominate grooves.^{7,8} Upon further inspection, using chromoendoscopy and magnified colonoscopy, lesions may be risk-stratified by their overall size, mucosal characteristics, and pit pattern.

The use of chromoendoscopy, specifically using an indigo-carmin solution, may be utilized to further characterize gastrointestinal lesions.⁹ Nonpolypoid lesions may then be categorized by the Paris criteria, which expands on the Japanese Gastric Cancer Association of stomach cancers, and are categorized into five types (0–5).¹ The Paris criteria expand on type 0 lesions, which are described as superficial protruding or nonprotruding lesions. There are three subcategories, as described by the Endoscopic Classification Review Group: 0-I, 0-II, and 0-III. Protruding lesions are 0-I; 0-Is sessile, or 0-Ip pedunculated. Nonprotruding and nonexcavated lesions are 0-II; 0-IIa slightly elevated, 0-IIb flat, and 0-IIc slightly depressed. Excavated lesions (0-III) are subdivided into ulcerated, excavated, and depressed types (–Table 1).¹

In addition to the gross appearance of the mass, other characteristics can be used to predict risk of invasion. For

Table 1 Nonpolypoid polyp classification based on the Paris criteria

Classification	Definition
Type 0 lesions	Superficial protruding or nonprotruding lesions
0-I	Protruding lesions
0-Is	Protruding, sessile lesion
0-Ip	Protruding, pedunculated lesion
0-II	Nonprotruding, nonexcavated lesions
0-IIa	Nonprotruding, slightly elevated lesion
0-IIb	Nonprotruding, flat lesion
0-IIc	Nonprotruding, slightly depressed lesion
0-III	Excavated lesions, ulcerated or depressed

example, the nonlifting sign can macroscopically confirm the extent of invasion into the submucosa. To characterize a lesion as lifting or nonlifting, saline is injected into the submucosa thereby turning a flat polyp into a slightly raised polyp. If the base of the lesion does not elevate, there is a higher risk of submucosal involvement.¹⁰

Using magnified colonoscopy, endoscopists can also assess the pit pattern, which has been demonstrated in multiple studies to correlate with histological structure.¹¹ Pits, also known as the orifices of the colonic crypts, are divided into six groups that predict the histological structure of the lesions. Type I pits are round and regular. Type II pits are larger and star-shaped or onion-like. Type III pits are elongated and large. Commonly associated with adenomas, type III pits are small or short, and tend to be found in early cancers. Type IV pits are branched and long, and are also associated with adenomas. Type V pits are very irregular and associated with intramucosal cancer or high-grade dysplasia (► **Table 2**). The progression of pit pattern is associated with increased incidence of neoplastic change.¹²

Once the categorized lesion is excised, pathologists can complete the assessment of the lesion, which subsequently determines the need for further surgical intervention. The depth of invasion currently correlates with risk of lymph node metastasis.^{13,14} Specifically, a high correlation exists between submucosal invasion of less than 1,000 μ m (1 mm) and an absence of lymph node metastasis.¹³ Pathologists use the depth into the submucosa to decide the depth of invasion.

Sm1 is defined as a focal extension to the superficial submucosa, Sm2 is the penetration of the lesion to the midsubmucosal layer, and Sm3 is the extension through the submucosal layer to muscularis propria.^{15,16} Pathologists must also adhere to the Vienna classification system, a histopathologic tumor classification designed to standardize pathological reviews of all gastrointestinal biopsy specimens.^{15,17} If grade 1 is negative for neoplasia/dysplasia, follow-up is not required. If grade 2 is definite for neoplasia/dysplasia, follow-up is recommended. If grade 3 is noninvasive low-grade neoplasia (low-grade adenoma/dysplasia), endoscopic resection or follow-up is indicated. Grade 4 is noninvasive high-grade dysplasia, which is divided into 4.1, a high-grade adenoma/dysplasia; 4.2, a noninvasive carcinoma (carcinoma in situ); and 4.3, a suspicion of invasive carcinoma. Endoscopic or surgical local resection is indicated in these specimens. Grade 5 is invasive neoplasia, divided into 5.1 intramucosal carcinoma, and 5.2 submucosal carcinoma or beyond. Surgical resection is indicated for these individuals (► **Table 3**).

Using the above gross, magnified, and histopathologic descriptions, the endoscopist decides whether EMR or ESD would offer the appropriate complete therapeutic resection. Both techniques are described below.

Endoluminal Mucosal Resection

EMR is indicated for lesions involving the mucosa, specifically nonpolypoid, neoplastic lesions with less than 20 mm diameter that are not removable by snare polypectomy.^{3,18} A successfully treated polyp, excised by EMR, may demonstrate high-grade dysplasia, well or moderately differentiated cells with no lymphatic or vascular involvement, with cancer-free resection margin, and with no massive submucosal involvement.¹⁹ Ip/Isp lesions have been excluded from EMR in studies; Kudo pit pattern III/V lesions were also excluded, due to risk of deep submucosal invasion and asymmetric lifting. In addition, Kudo crypt I/II lesions, since they were less likely to be malignant, and individuals with impaired coagulation were also excluded.⁵

To perform EMR, trained nurses, as well as endoscopists familiar with the technology are required. Once the appropriate equipment is available and assembled, the patient should be sedated by the physician in the manner with which the patient is comfortable. At our institution, we routinely use moderate sedation with a combination

Table 2 Classification of colonic polyp pit pattern

Classification	Pit pattern	Histopathologic association
Type I	Round and regular	Normal tissue
Type II	Larger, star-shaped or onion-like	Normal tissue
Type III	Elongated and large	Adenoma
Type IIIs	Small and short	Early carcinoma
Type IV	Branched long pits	Adenoma
Type V	Irregular	Carcinoma or dysplasia

Table 3 Vienna classification for histopathologic tumor classification

Grade	Definition	Follow-up
1	Negative for neoplasia/dysplasia	None
2	Definite neoplasia/dysplasia	Recommended
3	Noninvasive low-grade neoplasia	Endoscopic resection of follow-up
4.1	High-grade adenoma/dysplasia	Endoscopic or surgical resection
4.2	Noninvasive carcinoma	Endoscopic or surgical resection
4.3	Suspicion of invasive carcinoma	Endoscopic or surgical resection
5.1	Intramucosal carcinoma	Surgical resection
5.2	Submucosal carcinoma	Surgical resection

fentanyl/versed; general anesthesia, however, may also be used. Endoscopists may then proceed as usual; once a polyp is identified, using the method originally described by Kudo, the lesion is excised.²⁰ First, 2 to 5 mL of 0.5% indigo carmine is flushed down the side port to delineate contour and morphology of the lesion. Magnification colonoscopy and crystal violet washes are then used to identify and characterize invasive pit patterns.⁵ Hsu et al use the pure cut and hemoclip method.⁷ After characterization of the lesions, 5 to 20 mL of normal saline is injected into the submucosal layer, using a standard 25 G injection needle inserted beside the lesion base. The lesion is then completely ensnared with a spiked snare, and resected with a 40-W pure cutting current, then clipped for hemostasis.^{7,19,20} After irrigation of the residual mucosa, any residual tissue identified may then be resected piecemeal, using a similar strategy. If this is unsuccessful, surgery is recommended.⁵

Other options for EMR include EMR-C (special cap) and underwater EMR.⁸ EMR-C utilizes a prepositioned capped snare to encircle the lesion. This, however, has been associated with increased perforation, and is therefore now only used in the rectum, which is an extraperitoneal space.²¹ Binmoeller et al described underwater EMR, and noted the muscularis propria remained circular when filled with water, eliminating the need for submucosal injection during resection. This technique requires desufflation then instillation of 500 to 1,000 mL of water to fill the lumen. The resection is then performed with a snare on blended current.²²

Outcomes

Multiple studies have reported on the outcomes of EMR. The risk of perforation is 0 to 0.2%,^{5,6,19,23} while the risk of bleeding was 0 to 22%.^{5,6,19,23} These complications did not typically require further surgical interventions. There was, however, an increased risk for complications in patients of older age with larger polyp size. Morbidity did depend on the location, the number, and morphology of the polyps removed, and it was increased with the use of anticoagulation.⁷ Fortunately, no mortalities were reported in the literature.⁶

Interestingly, on histopathology evaluation of specimens biopsied before resection, a 44 to 70% likelihood of pathologic

upgrade was reported^{5,23} indicative of the importance of using EMR for larger lesions initially biopsied on screening colonoscopy. Recurrences varied in several reports, from 0 to 11%.^{6,24,25} As expected, recurrent lesions required additional endoscopic intervention.²⁴ The lesions that were likely to recur were primarily large and therefore had a higher risk of harboring dysplastic and malignant changes.¹⁹ Few reported on overall survival, but one reported the median cancer-free survival rate for patients with adenocarcinoma was 27 months.²³

Endoscopic Submucosal Dissection

ESD was first described in gastric cancers in the management of lateral spreading tumors greater than 20 mm.^{26,27} This technique has recently been used for similar lesions in the lower gastrointestinal tract, primarily in Japan. Specifically, the Japan Colorectal ESD Standardization Implementation Working Group identified that any lesion difficult to remove en bloc should be considered a candidate for ESD. Lesions meeting this criteria included lateral-spreading tumors greater than 20 mm, pseudodepressed lateral-spreading tumors, lesions showing a Vi-type pit pattern or lesions 0-I with suspicion of adenocarcinoma, post-EMR recurrences,²⁸ or any lesion that needed en bloc resection.²⁹ It is also used in lesions at the anal canal, ileocecal valve, and appendiceal orifice.^{8,30}

The materials used in the EMR are similar to those needed to perform a successful ESD, including a tip-transparent hood, which provides the necessary tension for excision on the submucosal layer. A high-frequency power supply is needed with Endocut (Erbe Vio, Marietta, GA). To elevate the lesion, sodium hyaluronate diluted with indigo carmine and epinephrine is injected in the submucosa. A hook knife is then used for the mucosal incision, proceeding from the incised side to the nonincised side. The submucosal dissection is then completed with an insulated tip knife. Hemostasis is achieved with small cup hemostatic forceps with coagulation.^{28,29}

Outcomes

The goal of ESD is to reach R0 resection; several trials have reported rates from 70.5 to 90.3% in the colon,^{28,31,32} and 53 to 63% in the rectum.^{33,34} Bleeding complications occurred in 0 to 2% of patients with colon resections, and 13 to 28.6% in

the rectal resections,^{33,34} while perforations occurred 4 to 10% in the colon^{28,31,32} and 5.7 to 18% in the rectum.^{33,34} These results suggest colonic ESD is likely safer and more efficient than rectal ESD. Recurrence was low, at 0 to 1.8%,^{28,31} and only one death occurred in the colonic ESD sample population.³¹ A 2.8 to 7% recurrence rate in rectal lesions was noted within 3 months of original colonoscopy. Despite the higher recurrence rate, specifically in rectal lesions, there was a reported reduction from 20 to 1% in the need for surgery for rectal lesions after the introduction of ESD.³⁰ ESD may therefore lead to decreased health care costs by the reduction of surgical interventions. With the advent of TEM, however, rectal lesions can be removed in full-thickness, and the surgical wound can be closed. This technique is described below.

Transanal Endoscopic Microsurgery

TEM has become the preferred treatment for large rectal adenomas, but has also been used for low-risk pT1 rectal adenocarcinoma, invasive rectal adenomas with palliative intent.³⁵

TEM utilizes a 40-mm operating rectoscope that is sealed with an airtight face piece. Carbon dioxide is then infused to distend the rectum. Laparoscopic instruments are commonly used.³⁶ TEM has been demonstrated to have a high rate of complete resection with disease-free margins, which is strictly related to recurrence.³⁷ When TEM is compared with ESD, RO resection was achieved more commonly in TEM, and patients who had undergone ESD were more frequently referred to surgery.³⁸ TEM, when compared with transanal excision, was found to have a shorter operative time, and, as expected when compared with formal rectal resection, was associated with shorter hospitalization time and less mortality.^{39,40} While the recurrence rates after TEM procedures vary, they are low overall. Risk factors for recurrence include pT stage, Sm stage, and tumor grading.⁴¹ Complications associated with TEM occurred in approximately 9% of patients, and included bleeding, dehiscence, rectovaginal fistula, and rectovesical fistula,⁴¹ which are still lower than those reported with standard surgical intervention.⁴⁰

Future Directions

In conclusion, the outcomes from endoscopic techniques, including EMR and ESD support their use in the appropriate setting. As expected, surgery continues to evolve and benefit from the development of new endoscopic techniques. NOTES has stemmed from the marriage of endoscopy and laparoscopic surgery as a means of treating larger lesions without large abdominal incisions. This technique was first utilized in the transgastric abdominal exploration and liver biopsies by Kalloo et al.⁴² It has currently been expanded to gynecologic procedures, cholecystectomies, and appendectomies. While there is limited data in its application for colorectal surgery, Xingmao et al compared laparoscopic sigmoidectomies with natural orifice specimen retraction versus open retrieval and found less bleeding, faster return of bowel function, and fewer

complications with equivalent operating room time and days of hospitalization.⁴³ Future studies, however, are indicated to prove NOTES is a viable approach for resection of colorectal carcinomas.

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References

- 1 Endoscopic Classification Review Group. Update on the Paris classification of superficial neoplastic lesions in the digestive tract. *Endoscopy* 2005;37(6):570–578
- 2 Alves A, Panis Y, Manton G, Slim K, Kwiatkowski F, Vicaute E. The AFC score: validation of a 4-item predicting score of postoperative mortality after colorectal resection for cancer or diverticulitis: results of a prospective multicenter study in 1049 patients. *Ann Surg* 2007;246(1):91–96
- 3 Waye JD. Endoscopic mucosal resection of colon polyps. *Gastrointest Endosc Clin N Am* 2001;11(3):537–548, vii
- 4 Kudo Se, Lambert R, Allen JI, et al. Nonpolypoid neoplastic lesions of the colorectal mucosa. *Gastrointest Endosc* 2008;68(4, Suppl): S3–S47
- 5 Hurlstone DP, Cross SS, Drew K, et al. An evaluation of colorectal endoscopic mucosal resection using high-magnification chromoscopic colonoscopy: a prospective study of 1000 colonoscopies. *Endoscopy* 2004;36(6):491–498
- 6 Su MY, Hsu CM, Lin CJ, et al. Endoscopic treatment of colorectal neoplasms: a simple and safe procedure to lower the incidence of colorectal cancers. *Dig Dis Sci* 2008;53(5):1297–1302
- 7 Hsu CM, Ho YP, Lien JM, et al. Endoscopic mucosal resection using a pure cut and hemoclip method for colonic nonpolypoid neoplasms. *Chang Gung Med J* 2003;26(8):586–591
- 8 Sanchez-Yague A, Kaltenbach T, Raju G, Soetikno R. Advanced endoscopic resection of colorectal lesions. *Gastroenterol Clin North Am* 2013;42(3):459–477
- 9 Kudo S, Kashida H, Nakajima T, Tamura S, Nakajo K. Endoscopic diagnosis and treatment of early colorectal cancer. *World J Surg* 1997;21(7):694–701
- 10 Kobayashi N, Saito Y, Sano Y, et al. Determining the treatment strategy for colorectal neoplastic lesions: endoscopic assessment or the non-lifting sign for diagnosing invasion depth? *Endoscopy* 2007;39(8):701–705
- 11 Kudo S, Rubio CA, Teixeira CR, Kashida H, Kogure E. Pit pattern in colorectal neoplasia: endoscopic magnifying view. *Endoscopy* 2001;33(4):367–373
- 12 Tung SY, Wu CS, Su MY. Magnifying colonoscopy in differentiating neoplastic from nonneoplastic colorectal lesions. *Am J Gastroenterol* 2001;96(9):2628–2632
- 13 Mou S, Soetikno R, Shimoda T, Rouse R, Kaltenbach T. Pathologic predictive factors for lymph node metastasis in submucosal invasive (T1) colorectal cancer: a systematic review and meta-analysis. *Surg Endosc* 2013;27(8):2692–2703
- 14 Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. *Dis Colon Rectum* 2002;45(2):200–206
- 15 Schlemper RJ, Riddell RH, Kato Y, et al. The Vienna classification of gastrointestinal epithelial neoplasia. *Gut* 2000;47(2):251–255
- 16 Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. *Gastroenterology* 1985;89(2):328–336

- 17 Dixon MF. Gastrointestinal epithelial neoplasia: Vienna revisited. *Gut* 2002;51(1):130–131
- 18 Tanaka S, Haruma K, Oka S, et al. Clinicopathologic features and endoscopic treatment of superficially spreading colorectal neoplasms larger than 20 mm. *Gastrointest Endosc* 2001;54(1):62–66
- 19 Su MY, Hsu CM, Ho YP, et al. Endoscopic mucosal resection for colonic non-polypoid neoplasms. *Am J Gastroenterol* 2005;100(10):2174–2179
- 20 Kudo S. Endoscopic mucosal resection of flat and depressed types of early colorectal cancer. *Endoscopy* 1993;25(7):455–461
- 21 Inoue H, Kawano T, Tani M, Takeshita K, Iwai T. Endoscopic mucosal resection using a cap: techniques for use and preventing perforation. *Can J Gastroenterol* 1999;13(6):477–480
- 22 Binmoeller KF, Weilert F, Shah J, Bhat Y, Kane S. “Underwater” EMR without submucosal injection for large sessile colorectal polyps (with video). *Gastrointest Endosc* 2012;75(5):1086–1091
- 23 Ahmad NA, Kochman ML, Long WB, Furth EE, Ginsberg GG. Efficacy, safety, and clinical outcomes of endoscopic mucosal resection: a study of 101 cases. *Gastrointest Endosc* 2002;55(3):390–396
- 24 Wang AY, Ahmad NA, Zaidman JS, et al. Endoluminal resection for sessile neoplasia in the GI tract is associated with a low recurrence rate and a high 5-year survival rate. *Gastrointest Endosc* 2008;68(1):160–169
- 25 Barendse RM, van den Broek FJ, Dekker E, et al. Systematic review of endoscopic mucosal resection versus transanal endoscopic microsurgery for large rectal adenomas. *Endoscopy* 2011;43(11):941–949
- 26 Muto M, Miyamoto S, Hosokawa A, et al. Endoscopic mucosal resection in the stomach using the insulated-tip needle-knife. *Endoscopy* 2005;37(2):178–182
- 27 Oka S, Tanaka S, Kaneko I, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. *Gastrointest Endosc* 2006;64(6):877–883
- 28 Tanaka S, Oka S, Kaneko I, et al. Endoscopic submucosal dissection for colorectal neoplasia: possibility of standardization. *Gastrointest Endosc* 2007;66(1):100–107
- 29 Tanaka S, Oka S, Chayama K. Colorectal endoscopic submucosal dissection: present status and future perspective, including its differentiation from endoscopic mucosal resection. *J Gastroenterol* 2008;43(9):641–651
- 30 Hotta K, Saito Y, Fujishiro M, et al. Impact of endoscopic submucosal dissection for the therapeutic strategy of large colorectal tumors. *J Gastroenterol Hepatol* 2012;27(3):510–515
- 31 Fujishiro M, Yahagi N, Kakushima N, et al. Outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms in 200 consecutive cases. *Clin Gastroenterol Hepatol* 2007;5(6):678–683, quiz 645
- 32 Repici A, Hassan C, De Paula Pessoa D, et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. *Endoscopy* 2012;44(2):137–150
- 33 Rahmi G, Hotayt B, Chaussade S, et al. Endoscopic submucosal dissection for superficial rectal tumors: prospective evaluation in France. *Endoscopy* 2014;46(8):670–676
- 34 Fujishiro M, Yahagi N, Nakamura M, et al. Endoscopic submucosal dissection for rectal epithelial neoplasia. *Endoscopy* 2006;38(5):493–497
- 35 Endreseth BH, Myrvold HE, Romundstad P, Hestvik UE, Bjerkset T, Wibe A; Norwegian Rectal Cancer Group. Transanal excision vs. major surgery for T1 rectal cancer. *Dis Colon Rectum* 2005;48(7):1380–1388
- 36 Saclarides TJ, Smith L, Ko ST, Orkin B, Buess G. Transanal endoscopic microsurgery. *Dis Colon Rectum* 1992;35(12):1183–1191
- 37 Allaix ME, Arezzo A, Cassoni P, Famiglietti F, Morino M. Recurrence after transanal endoscopic microsurgery for large rectal adenomas. *Surg Endosc* 2012;26(9):2594–2600
- 38 Arezzo A, Passera R, Saito Y, et al. Systematic review and meta-analysis of endoscopic submucosal dissection versus transanal endoscopic microsurgery for large noninvasive rectal lesions. *Surg Endosc* 2014;28(2):427–438
- 39 de Graaf EJ, Burger JW, van Ijsseldijk AL, Tetteroo GW, Dawson I, Hop WC. Transanal endoscopic microsurgery is superior to transanal excision of rectal adenomas. *Colorectal Dis* 2011;13(7):762–767
- 40 Langer C, Liersch T, Süß M, et al. Surgical cure for early rectal carcinoma and large adenoma: transanal endoscopic microsurgery (using ultrasound or electrosurgery) compared to conventional local and radical resection. *Int J Colorectal Dis* 2003;18(3):222–229
- 41 Morino M, Allaix ME, Caldart M, Scozzari G, Arezzo A. Risk factors for recurrence after transanal endoscopic microsurgery for rectal malignant neoplasm. *Surg Endosc* 2011;25(11):3683–3690
- 42 Kalloo AN, Singh VK, Jagannath SB, et al. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointest Endosc* 2004;60(1):114–117
- 43 Xingmao Z, Haitao Z, Jianwei L, Huirong H, Junjie H, Zhixiang Z. Totally laparoscopic resection with natural orifice specimen extraction (NOSE) has more advantages comparing with laparoscopic-assisted resection for selected patients with sigmoid colon or rectal cancer. *Int J Colorectal Dis* 2014;29(9):1119–1124