The results and limitations of endoscopic submucosal dissection for colorectal tumors

T. Toyama1, M. Man1, D. Ivanov3, T. Sanuki1, Y. Morita2, H. Kutsumi2, H. Inokuchi2, T. Azuma2
1, 2Department of Endoscopy and Gastroenterology, Kobe University Hospital, Kobe, Japan
3Clinical Center of Vojvodina, Clinic for Abdominal, Endoscopic and Transplant Surgery, Novi Sad, Serbia

INTRODUCTION

The development of endoscopic submucosal dissection (ESD) enables en-block resection of the lesions which were difficult to be removed by the conventional endoscopic mucosal resection (EMR). EMR is a so called advanced polypectomy using a snare. On the other hand, we can say that ESD is endoscopic surgery because we incise the mucosal layer around the lesion and dissect the submucosal layer with endo knives. Theoretically, ESD enables en-block resection of a lesion regardless of its size and location. However, ESD is associated with higher technical difficulty, longer procedure time, and increased risk of complication. The risk of complication of colorectal ESD is thought to be much higher than gastric ESD because of the thin wall and narrow lumen. Recently, colorectal ESD can be performed rather easy and surely when we choose the method that is appropriate to the anatomical characteristic. Above all, the rectum has comparatively thick muscle layer and wide lumen, so it is rather easy to approach by ESD. Moreover, the invasion by the operation of the rectum is serious. Therefore, the rectum is the most proper location for the ESD. In this report, we describe an outline of the methods, treatment results, indications and limitations of colorectal ESD.

PATIENTS/ MATERIALS AND METHODS

We introduced ESD from June 2002. In the colorectum, we assume the lesions larger than 20mm to be the indication for ESD, and have resected 361 lesions (adenoma; 118, mucosal cancer; 177, submucosal cancer; 66) by July 2007.

THE SUITABLE LESIONS FOR THE ENDOSCOPIC TREATMENT

The curability is the major point of indication of ESD; whether with or without lymphnode metastasis. ESD is the local resection, so its objects are the lesions without
metastasis. In the Colorectum, these lesions are concretely as below, 1) Adenomas 2) Intramucosal cancers 3) Minimally invasive submucosal cancers (invasion depth 1000m, well and modelately differentiated type, no lymphovascular invasion) 1).

THE DEVICES FOR ESD AND THEIR CHARACTERISTIC

The development of the devices has enabled us to perform ESD. Especially, the development of electro surgical generator and local injection solution, and the invention of endo knives have played a great role. Endo knives (Fig.1)

Flex knife (Olympus Optical Co, Ltd)\(^2,3\) is a dull and round tipped knife with a stopper at the tip of the sheath, and the sheath is flexible to absorb rapid change of the depth of the knife. The length is also shortened optionally, it is suitable for the colorectum with thin wall. On the contrary, it is difficult to dissect the submucosal layer with severe fibrosis, and it is often stressful to regulate the length of the knife.

Flush knife (Fujinon Optical Co, LTD)\(^4,5,6\) is a characteristic knife with a needle of 0.5 mm in diameter and 5 projecting parts of 1, 1.5, 2, 2.5 and 3 mm in length. For the colorectal ESD, the 1.5 mm (or 2 mm) type is suitable for the mucosal incision, and the length of 1.5 mm (or 1 mm) type is for the submucosal dissection. The knife is set up to the projection length only by pushing out the needle handle, which is maintained during the procedure. Using the tip of the sheath as a guard, the knife enables safe and easy handling. Protecting the lesion and the muscle layer with the tip part of the sheath, the submucosal layer can be divided, and the severe fibrosis can be dissected easily. Emitting a jet of water from the tip of a sheath enables lavage of the viewing field, and submucosal local injection without replacement of operative instruments, which led to very efficient treatment. Flush knife was introduced after March 2003, and now it is used for the all colorectal ESD, and good results are provided.

Hook knife (Olympus Optical Co, Ltd)\(^7,8\) is a device in which the tip of a Needle knife is bent at an angle of 90 degrees to be hook shaped. The tip can be rotated and fixed in arbitrary directions. The handling is complicated but the knife is very safe because it can hook the object to safer direction.

Insulation-tipped (IT) knife (Olympus Optical Co, Ltd)\(^9,10\) is a needle knife with the ceramic ball at the tip of the knife for the prevention of perforation. We cannot dissect with the tip, so a handling to force for a blade is necessary. However, the handling should be parallel to the muscle layer to prevent the perforation and the damage of the lesion, so there is little usable situation of IT-knife in the colorectum, especially colon, with many folds and flexions. Moreover, because of thin wall, the IT knife will often roll up the muscle layer and the perforation easily occurs in the colorectum. The use of the IT knife in colorectum is undesirable. B-knife (Zeon Medical Inc) is a needle knife of the bipolar structure. Theoretically, there is little heat damage to the deep part of the tissues. B-knife is thought to be safe for the organs with thin wall.

\(\text{FIGURE 1} \quad \text{DEVELOPMENT OF ENDO-KNIVES BASED ON THE CONVENTIONAL NEEDLE KNIFE, SEVERAL ENDO-KNIVES FOR ESD HAVE BEEN DEVELOPED.}\)

\(\text{FIGURE 2} \quad \text{HUGE RECTAL TUMOR.}\)
not provided. In ESU such as ICC or VIO (ERBE Elektromedizin GmbH) used for ESD, the voltage is automatically controlled to become always constant during the incision, so uniform and reproducible quality of incision can be obtained. Furthermore, these ESU carrying Endo-Cut mode and various coagulation mode support the suitable condition of ESD.

ATTACHMENT AND TRANSPARENT HOOD

An attachment is used to keep the clear visual field when getting into the flexion and the submucosal layer. It is indispensable for the esophageal and colorectal ESD.

Small-caliber tip transparent (ST) hood (Fujinon Optical Co, LTD) is a hood that the tip is narrow in the conical shape, and it can secure the field of vision in the slight crack. Because, the visual field is small and the hood is easy to be smudged, it is not general-purpose.

HEMOSTATIC FORCEPS

Effective hemostasis and the prevention of bleeding are also indispensable to safe procedure. Hot biopsy forceps was misappropriated at first, but exclusive hemostatic forceps (Coagulasper Olympus Co, LTD) is already marketed. Current conduction after the grasping and retracting the vessel is of importance to prevent the delayed perforation.

METHODS OF ESD

MARKING

We place markings around the lesion to clarify the confines of the lesion in stomach and esophagus. However, the border of the colorectal lesion is clear, there was no need to place marking in the colon and the rectum. (fig. 2)

LOCAL INJECTION

The solution is injected into the submucosal layer, to create the protrusion to the luminal side. Diluted sodium hyaluronate is chosen for the colorectum which has thin wall in order to maintain the protrusion during the procedure.

MUCOSAL INCISION

The circumferential incision around the lesion is performed using endo knives.

SUBMUCOSAL DISSECTION

After the additional local injection, the submucosal layer is dissected.

COLLECTION AND THE HISTOPATHOLOGICAL DIAGNOSIS

The removed lesion is collected and carefully examined histopathologically.

The arts of procedure in colorectal ESD (Fig. 3) 4,5,6,11,12,13,14,15

First, the mucosal incision from the anal side is to be performed, then, the submucosal dissection has to be performed until the attachment could get into the submucosal layer. This procedure is particularly important for the lesions which extend over the folds, and also the lesions which are at the location where the muscle layer rises perpendicularly.

By incision and trimming to the anal (proximal) side of the lesion without performing the mucosal incision of the oral (distal) side, the lesion is pulled into the oral side and the crack to approach the submucosal layer is easily produced. On the contrary, when we first incise and trim the oral (distal) side of the lesion, the tension of mucosa on the oral side disappears and the lesion does shift to the anal side.

Once we have got into the submucosal layer, we appropriately add the mucosal incision from the lateral side to the oral side, and proceed with the dissection.

FIGURE 2 E: RESECTED SPECIMEN. THE DIAMETER OF TUMOR 155X140 MM,

FIGURE 2 F: VIEW OF 3 MONTHS AFTER ESD.
When the dissection is proceeded, the lesion hangs down and gets possible to dissect extremely efficiently. We also change the posture of the patient appropriately, and use the gravity effectively. As for the important thing, when two-third of the dissection is performed, we must complete the mucosal incision and trimming before the lesion completely turns over into the oral (distal) side and covers the object. We go ahead with the dissection from the anal (proximal) side again after the completion of this procedure. The final dissection is sometimes accompanied with difficulty. However, if the trimming of the oral side is done to enough depth, the submucosal layer extends by the weight of the lesion, and we should see the incision border of the distal (oral) side. Excision is completed surely when we perform the last part of the dissection to trace this incision border.

LIMITATION AND "MUSCLE RETRACTING SIGN"

There is a limitation for the diagnosis of the invasion of the colorectal tumor, especially the lesion with protrusion larger than 3 cm, even if we make full use of barium enema, endoscopic ultrasonography, and magnifying endoscope. Sometimes we cannot remove the lesions which seem to be resectable because of the deep wall invasion, on the other hand, we can often remove the lesions easily even with huge protrusion.

In the case of the massively invasive submucosal cancer or invasive cancer, muscle layer might be retracted to the lesion at the invaded portion. when the retracted muscle is recognized, the procedure should be discontinued because the continuation of the procedure raises the risk of perforation and it means the lesion could be out of the indications. We call this phenomenon "muscle retracting sign". When we perform ESD for the lesions with the large sessile protrusion, we prepare for the surgical operation. When we recognize "muscle retracting sign", we cope by performing the radical surgical resection as soon as possible, so that the lesion does not become necrotic.

RESULTS

The overall en-block complete resection rate was 95.2% (355/373). When we omit 12 cases that muscle retracting sign had been seen and procedure was discontinued, the rate of en-block complete resection was 98.3%. The median tumor size was 30 mm (range: 6-158), and the median specimen size was 40 mm (range: 16-165), and the median procedure time was 58 min. (range: 15-335). As for the complication, the postoperative bleeding occurred in 0.8 % (3 cases: no blood transfusion is needed). The intraoperative perforation occurred in 1.9 % (6 cases: 5 cases were treated conservatively, 1 case was treated surgically) and the postoperative perforation occurred in 1 case (0.3%) treated surgically. Furthermore, after the induction of the Flush knife, the tackling to the lesion with fibrosis becomes easy. The frequency of combination use of devices was decreased and the procedure time was shortened particularly in the difficult cases.

DISCUSSION

Even if endoscopic treatment can remove such large lesions, it is only local resection. The suitable lesions are limited to those without metastasis, and in the colorectum, the lesions are as mentioned above. In the stomach, these lesions are concretely as below, 1) Intramucosal cancers, differentiated type, no lymphovascular invasion, and no ulceration, irrespective of tumor size, 2) Intramucosal cancers, differentiated type, no lymphovascular invasion, and tumor less than 3cm in size, irrespective of ulceration findings, 3) Minimally invasive submucosal cancers (invasion depth 500 m), differentiated type, no lymphovascular invasion, and tumor less than 3cm in size. In the esophagus, these lesions are intramucosal cancers (invasion depth m1-m2), 2/3 around the lumen. There is limitation for the preoperative diagnosis too, so we must judge whether curative resection has been done by the correct histopathological diagnosis of the specimen. Especially, the judgment such as the depth of submucosal invasion and lymphovascular invasion is crucial. The conventional EMR forced many lesions to be removed by the piecemeal resection. The piecemeal resection has the problems that many recurrences often occur by the misjudgment of the margin, and correct histopathological diagnosis is difficult by the damage of specimen. The meaning that ESD has enabled en-block resection is extremely great. The problems of ESD will be the high technical difficulty and long procedure time, and high frequency of the complication. In the colorectum, the mu cosa is easy to cut, and a little bleeding occurs, there is not so much difficulty to perform smooth dissection if the good field of vision is provided.
The tumor size and location do not influence the degree of difficulty, and only make the difference of the procedure time. The difficult cases of colorectal ESD are the lesions with severe fibrosis. The most of those are non-granular type of lateral spreading tumor (LST-NGs). Also, the submucosal layer of LST-NGs is thin, and the lesions often extend over the folds and the flexion. Therefore, LST-NGs are the lesions which are the most difficult for ESD. In case of the severe fibrosis, it is not easy to keep the clear field of vision with the normal attachment. In addition, it is difficult to dissect the severe fibrosis with Flexknife because its tip is dull and sheath is soft. However it is not so difficult with Flush knife. With Flush knife, operators can protect the muscle layer and the lesion and go into the submucosal layer with the tip of the sheath.

The major complication of ESD consists of the perforation and bleeding, and it is distributed for the intraoperative and postoperative. Although the frequency depends on the operator and institution, it is generally regarded as around 3-10%.

Above all, the perforation is the most serious complication, and the recognition is widely spreads out that the frequency of the perforation is extremely higher in colorectal ESD than in the gastric ESD. However, the frequency is actually high when IT knife is used, but it is not so high when operators use the devices which dissect with the tip, such as Flush knife. Furthermore, the intraoperative perforation by ESD is pinhole shaped, and conservative treatment is possible to close the hole by the clip. If the transmural burn happens even if there is no intraoperative perforation, the necrotic region may fall off to cause the delayed perforation. This is the same phenomenon that has been reported as post polypectomy coagulation syndrome caused by the resection with the snare and hot biopsy forceps. We experienced the delayed perforation in one case that the operator coagulated too much the blood vessels on the bottom of the ulcer. Histopathologically, in the resected specimen, the muscle layer was partly missing, and the remained muscle layer fell into the necrosis widely by the coagulation. After the measures to conduct the current after grasp and traction with small hemostatic forceps, there is no delayed perforation. The postoperative bleeding is experienced in the case of the lesion on the ileocecal valve, rectum, and anal canal and recognized with the bloody diarrhea. We have no clinically troublesome case, and there was no patient who needed the blood transfusion. There were only two cases that needed coagulation with hemostatic forceps.

ESD needs not only the technique of the operator, but also the cooperation with the assistant. It is necessary for the assistant to understand the whole procedures of ESD, and also, the characteristic and the use of devises. For the induction of ESD, the conference, study group, and live demonstration should be used to collect knowledge. The smooth introduction and the training system of ESD are the important themes in the future.

CONCLUSION

By the development of ESD, endoscopic treatment has met a new era. Such lesions that are diagnosed to have no lymph node metastasis can be removed completely by this method, which is expected to greatly contribute to the QOL of the patients. Even in the colorectum, ESD can be performed safely by the proper choice of the devices and appropriate resection strategy. However, there is a limitation for the preoperative diagnosis of the lesions with
SUMMARY

REZULTATI I OGRANIČENJA ENDOSKPSKE SUBMUKOZNE DISEKCIJE KOLOREKTALNIH TUMORA

Kolorektalni tumor koji se mogu lećiti endoskopski su tumori bez metastazas u limfnim čvorovima, kao što su adenomi, intramukozni karcinomi i minimalno invazivni submukozni karcinomi (dubina invazije manja od 1000m, dobro i srednje diferentirani, bez limfovaskularne invazije). Nova endoskopska tehnika, endoskopska submuko- zna disekcija (ESD) omogućava "en-bloc" resekciju tu- mora bez obzira na njegovu veličinu i lokalizaciju. U cilju lakšeg, sigurnijeg i efikasnijeg izvodjenja ESD-a izumeli smo "water jet" endoskopske noževe kratkog vrha ("Flush no"). Ovaj nož izbacuje mlaz vode sa svog vrha i time omogućava disekciju submukoznog sloja bez potrebe zamene instrumenata a to vodi efikasnijem tretmanu. "Flush no" je posebno efikasan u uklanjanju tumora don- jeg rektuma i analnog kanala, regija sa mnogo krvnih sudova. Endoskopskom submukoznom disekcijom lećili smo 361 kolorektalni tumor u periodu od juna 2002. do jula 2007. godine sa stopom kompletne, "en-bloc" resekre- cije tumora od 98,3%. Znak "povlačenja mišiće" je vidjen u 12 slučajeva. Ovaj znak ukazuje na potrebu odustajanja od dalje endoskopske submukozne disekcije, ali ga je nemoguće otkriti preoperativno. Postoperativno kvarećenje se javilo u 0,8% slučaja (3 puta: bez potrebe za transfuzi- jom). Intraoperativna perforacija se desila u 1,9% (6 slučajeva: 5 puta lečeno konzervativno, a jednom hirurški) a kod slučaja postoperativne perforacije (0,3%) lečenje je završeno hirurški. Endoskopska submukozna disekcija je izuzetno efikasan način lečenja kolorektalnih tumora, i uz pravilan odabir instrumenata i strategije, može se izvesti bezbedno.

REFERENCES


