Usefulness of IT knife nano for endoscopic submucosal dissection of large colorectal lesions

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Abstract

Aim : **Endoscopic submucosal dissection (ESD) is currently widely conducted for the treatment of early gastrointestinal cancers. Due to the characteristic anatomy of the large intestine, needle- tip type devices such as Dual knife are mainly used in colorectal ESD. On the other hand, the non- needle-tip type IT knife is a unique device with an insulated tip, and has been reported to be safe, efficacious and speedy when used in gastric ESD. A new model of IT knife, IT knife nano, anticipated to be useful for esophageal and colorectal ESD has become available, but its usefulness has not been reported. Therefore, we performed this study to evaluate the usefulness of IT knife nano for ESD of large colorectal lesions.**

Methods : **Previous studies have shown that a tumor size of 40 mm or above significantly prolongs treatment time and is a factor of treatment difficulty. We selected colorectal lesions of 40 mm and above, and compared 32 lesions treated with Dual knife alone before IT knife nano was available (No-IT group) and 40 cases treated with IT knife nano as a second knife after IT knife nano became available (IT group). We assessed *en bloc* resection rate, complete *en bloc* resection rate, complication rate and treatment time.**

Results : **The *en bloc* resection rates in No-IT group and IT group were 100% and 97.5%, respectively, with no significant difference. The respective median treatment time was 70 min and 51 min, and was significantly shortened in IT group ($P < 0.05$). The respective rates of procedure- related perforation were 3.1% and 0% ; in IT group suggesting a tendency of reduced incidence.**

Conclusion : **Use of IT knife nano in ESD for large colorectal lesions achieves the same levels of efficacy and safety as conventional device, with the additional merit of shortening treatment time.** (Acta gastroenterol. belg., **2016**, 79, **186-190**).

Key words : IT knife nano, ESD, colon.

Introduction

Endoscopic submucosal dissection (ESD) is widely used as an endoscopic treatment for early gastrointestinal cancers (1-4). The procedure was initially used in the stomach, and its use has since been extended from the esophagus to the large intestine. In Japan, colorectal ESD also was approved for health insurance coverage in April 2012, and use of the procedure has continued to expand. With the recent technical advances in colorectal ESD and evolution of the devices, very good treatment results have been achieved (5-11). However, the procedure remains technically demanding and the rate of procedural incidents including perforation is relatively high (12-15). Especially in the large intestine, the thin intestinal wall increases the risk of perforation and associated peritonitis, while bending of the intestinal tract poses technical difficulties such as limited maneuverability of the endoscope (16-18). Moreover, a large tumor size has been reported to be a factor of treatment difficulty and requires long treatment time (18). Prolonged treatment time adds burden to the patient. Furthermore, use of sedative further increases the risk, and onset of peristalsis worsens the treatment environment putting extra burden on the operator and carer. It is important to be able to treat these tumors efficaciously and at the same time preserve safety.

In our hospital, we had been using needle-tip type devices such as Flex knife and Dual knife in colorectal ESD. When difficulties were encountered, such as when fibrosis was present and when the knife was perpendicular to the intestinal wall, the SB knife Jr was sometimes used in combination (19,20). Between 2006 and 2014, we performed a total of 454 colorectal ESD. When the ESD technique was first introduced, the Flex knife and Dual knife were used as the main devices, and the procedure was performed in principle using a single device. Comparison of treatment results over the years showed that the technique was stabilized from 2012, with *en bloc* resection rates of 95% and above, and perforation rates of 1% and below. Although we achieved good results with high *en bloc* resection rate and low procedural incident rate, the issue of long treatment time for large tumors remained.

Previous study has reported the efficacy and speedy treatment when using the IT knife 2 for gastric ESD (21). Recently IT knife nano, an improved model of IT knife suitable for use in organs with thinner wall such as the esophagus and colon, has become available. Our facility also adopted IT knife nano for colorectal ESD. However, in the colon where the mucosa is soft and tension is difficult to enhance, the IT knife nano is slightly inferior in circumferential incision. With the anticipation that it would be difficult to complete the resection using a single knife, we have used the IT knife nano as the second knife in combination with a needle-tip device. In addition, considering the cost of using the IT knife nano in all colorectal ESD, we have limited its use in large colorectal tumors only. Based on a previous report that the mean

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Submission date : 10/09/2015
Acceptance date : 27/11/2015

lesion size of colorectal ESD is 30 mm and that a lesion of 40 mm or greater is a factor of treatment difficulty,22 we conducted an evaluation of the efficacy and safety of the IT knife nano when used in colorectal ESD for lesions of 40 mm or above. In this study, we aimed to prove the usefulness of IT knife nano for ESD of large colorectal lesions.

Patients and methods

Patients

Between March 2006 and December 2014, we performed colorectal ESD in 454 patients at Chiba Cancer Center. We excluded the first 150 cases between March 2006 and March 2012, because our procedure in this term was unstabilized. We analysed our treatment results and found our procedure was stabilized at April 2012. And the target for analysis became consecutive 304 cases of colorectal ESD from April 2012. Among these patients, 72 cases with tumor diameters of 40 mm and above were studied. They comprised all 40 cases performed after the IT knife nano was introduced (IT group) and 32 cases performed before IT knife nano was used (No-IT group). Due to the high cost of using the device in all the colorectal ESD, IT knife nano was used only in large tumors as defined above. All patients provided written informed consent. The study was approved by the ethics committee of Chiba Cancer Center and carried out in accordance with the World Medical Association`s Declaration of Helsinki.

Indications for colorectal ESD

The indications for colorectal ESD were decided with reference to the proposal by the Japan Committee of Colorectal Endoscopic Submucosal Dissection Standardization. Among the lesions judged by endoscopy of requiring *en bloc* resection, the following lesions were indicated for colorectal ESD : nongranular laterally spreading tumors (LST-NG), especially the pseudo-depressed type ; type VI pit pattern lesion ; submucosal mildly invasive cancer ; large depressed type tumor ; large protruding lesion suspected to be cancer, intramucosal lesion with fibrosis in submucosal layer ; sporadic localized tumor with a chronic inflammatory background such as ulcerative colitis ; and localized residual cancer following endoscopic resection.

Devices used and technique

The ESD devices used were Dual knife (Olympus, Japan) which is a needle-tip type knife with a tip of 1.5 mm, and IT knife nano (Olympus, Japan) which is a knife with an insulated tip covering the needle and a metal disc at the back of the insulated tip (Figs. 1 and 2). The high frequency device used was VIO300D (ERBE, Germany). The settings for the Dual knife were Endocut I, Effect 3, Duration 3, and Interval 3 for mucosal incision ; and Swiftcoag 30 W and Effect 3 for submucosal dissection. The IT knife nano was used for submucosal dissection only, at settings of Swiftcoag 45 W and Effect 4. The IT knife nano was used in combination with the Dual knife in cases predicted preoperatively to have tumor diameters of 40 mm and above.

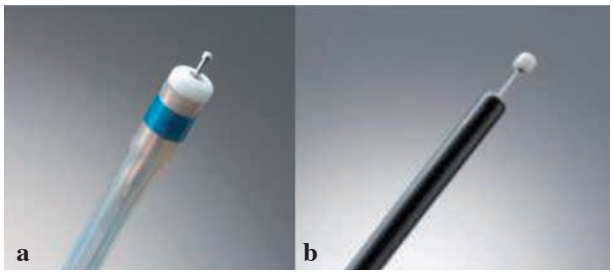

Fig. 1. — Electrosurgical knives used for colorectal endoscopic submucosal dissection (ESD) in the present study.
a : Dual knife has a knife length of 1.5 mm with a disc-shaped tip 0.3 mm in diameter. It is one of the general devices widely used in colorectal ESD. b : IT knife nano has an insulated tip with a small disc at the back of the tip and an metal arm. It is a modified model of the IT knife 2 used mainly in gastric ESD. IT knife nano is suited for organs with a thinner submucosa, such as the esophagus and large intestine.

Two endoscopists performed the ESD. Both were certified supervising doctors of endoscopy society in Japan and had performed over 700 ESD including esophageal, gastric and colorectal ESD. In the No-IT group, Dual knife alone was used. In the IT group, Dual knife was used as the first knife and IT knife nano as the second knife. After making a deep circumferential mucosal incision using the Dual knife, the IT knife nano was used to perform submucosal dissection.

Statistical analysis

The data are presented in percentage or median and range. Chi-square test was used to compare the *en bloc* resection rate and rate of procedural incidents between two groups. Mann-Whitney's U test was used to compare the treatment time between two groups. A p value less than 0.05 was considered to indicate statistical significance. Statistical analyses were performed using StateMate IV (ATMS, Japan).

Results

In all 304cases analyzed in this study, the overall *en bloc* resection rate was 97.6%, the complete *en bloc* resection rate was 96.2%, and the rates of procedural incidents were 2.8% for delayed bleeding and 0.7% for perforation.

Table 1 shows the clinical background of the No-IT group (n = 32) and the IT group (n = 40). No significant differences in tumor size, location, morphology, and histopathology were observed between the two groups. In regards of the histopathology, the number of mucosal

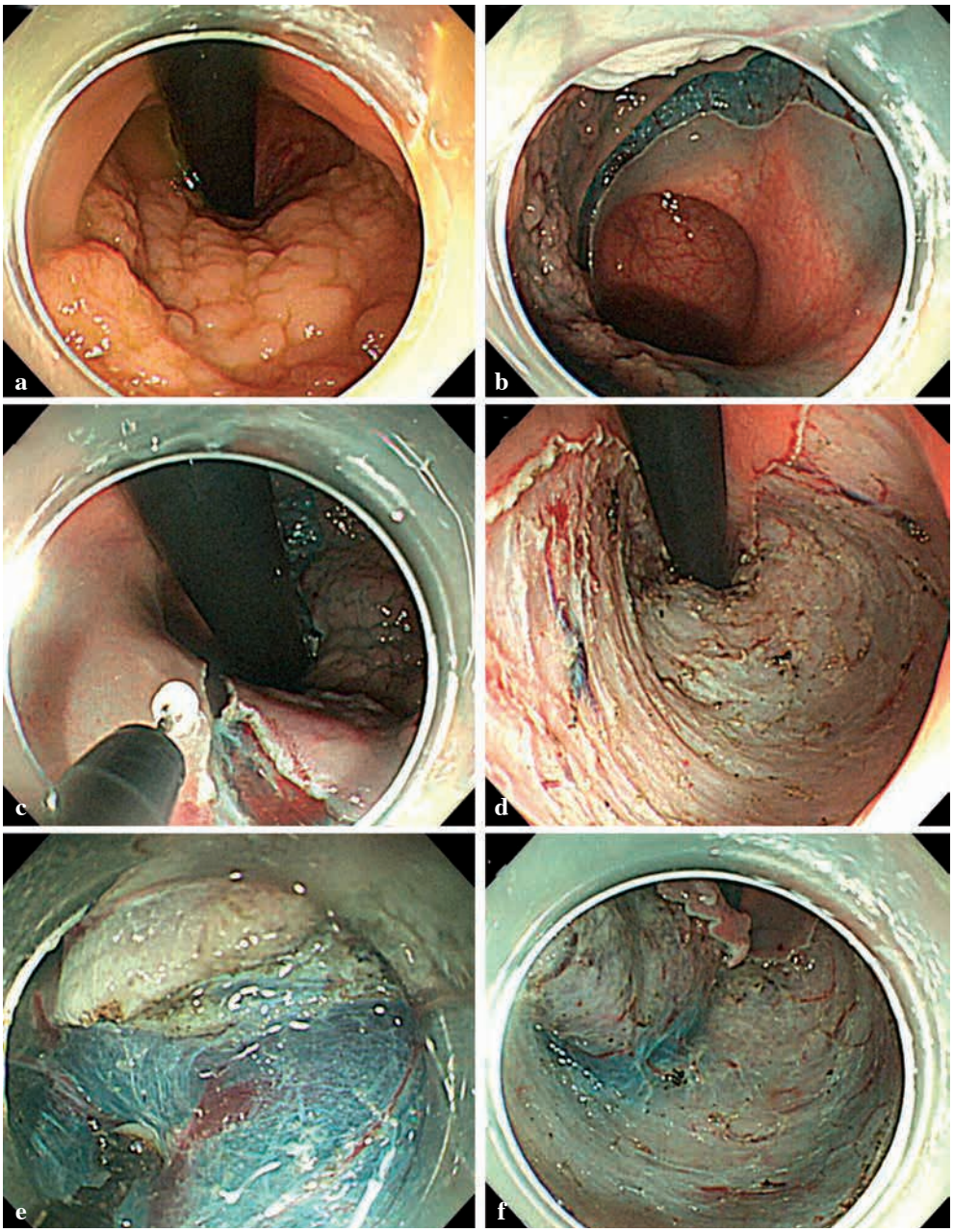

Fig. 2. — Endoscopic submucosal dissection (ESD) procedure.
a : The lesion is a large granular laterally spreading tumor (LST-G) of approximately 80 mm, extending from the lower rectum (Rb) to the anal canal. b : Circumferential incision is completed. c : After completion of incision, dissection using IT knife nano is started. d : Dissection is possible with almost no pre-coagulation of the submucosal vessels. e : Latter half of dissection. f : Dissection is completed. The procedure lasted 92 min.

cancer, submucosal cancer and adenoma were respectively 19 (60%), 2 (6%) and 11 (34%) in No-IT group and 20 (50%), 6 (15%) and 14 (35%) in IT group.

Table 2 shows the treatment results and the procedural incidents of the two groups. In the No-IT group, the *en bloc* resection rate was 100%, the complete *en bloc* resection rate was 100%, the median treatment time was 70 min (range ; 18 to 150 min), the median number of hemostatic clamp use was 4 (1 to 8), the procedure-related perforation rate was 3.1% and delayed bleeding rate was 7.5%. In the IT group, the e*n bloc* resection rate was 97.5%, the complete *en bloc* resection rate was 97.5%, the median treatment time was 51 min (range ; 24 to 170 min), the median number of hemostatic clamp use was 1 (0 to 3), the perforation rate was 0%, and the delayed bleeding rate was 9.4%. The delayed bleeding rate was higher than those of previous reports, because this study was dealing with larger lesions. Actually, delayed bleeding rate of our all cases was 2.8% which was lower than those of previous reports.

Table 1. — **Comparison of patient background of the group using (IT group) and the group not using IT knife nano (No-IT group)**

	No-IT group (N = 32)	IT group (N = 40)	
Median resection diameter <mm> (range)	40 (40-74)	45 (40-70)	N.S
Lesion location (rectum/colon)	11/21	17/23	N.S
Morphology (LST-G/NG/others)	26/5/1	29/2/0	N.S
Histopathology (Cancer/Adenoma/others)	21/11/0	26/14/0	N.S

Table 2. — **Comparison of treatment results of the group using IT knife nano (IT group) and the group not using IT knife nano (No-IT group)**

	No-IT group (N = 32)	IT group (N = 40)	
En-bloc resection rate <%>	100	97.5	N.S
Median treatment time <min> (range)	70 (18-150)	51 (24-170)	P < 0.001
Median number of hemostatic clamp use (range)	4 (1-8)	1 (0-3)	P < 0.001
Perforation range <%>	3.1	0	N.S
Delayed bleeding rate <%>	7.5	9.4	N.S

Use of IT knife nano significantly shortened procedure time. Although perforation rate did not differ significantly between two groups, use of IT knife nano resulted in no perforation in all cases.

Statistical analysis of the above data showed no significant differences in *en bloc* resection rate and complete *en bloc* resection rate between the No-IT group and IT group. However, the treatment time was significantly shorter in the IT group, and the number of hemostatic clamp use was also fewer in the IT group. Regarding procedural incidents, the delayed bleeding rates were slightly high since the tumors were larger than usual in this study, but there was no significant difference between two groups. The perforation rate was also not significantly different between two groups, but there was no perforation in all cases of the IT group, suggesting a tendency of reduced incidence compared to the No-IT group.

The following is a summary of the above. The settings of both groups were not different.

In the condition, the use of IT knife nano for colorectal ESD made the method more speedy and safer.

Discussion

Many reports mainly from Japan have indicated the efficacy of colorectal ESD (3-11). In the early stage of clinical application, standardization of the colorectal ESD procedure was considered difficult due to the high perforation rate and the technical complexity. Subsequently, with the evolution of devices and advances in technology, the perforation rate has decreased significantly and the procedure can now be performed more safely. Moreover, standardization has become possible (7). However, multiple factors contributing to treatment difficulty remain to be solved (16-18). Large tumor size is one of such factors that have to be conquered. While the efficacy and safety of colorectal ESD for large tumors have been reported, the long treatment time remains an issue. The difficulty increases especially for tumors exceeding 40 mm (18-22).

With this background, the IT knife nano with an insulated tip is anticipated to shorten treatment time while maintaining a high level of safety compared to the needle-tip type knifes currently used as the main device for colorectal ESD. For gastric ESD, IT knife 2 has been reported to be safe and allow speedy treatment (21).

Unlike the needle-tip type knife, the tip of the IT type knife has a round insulated tip that theoretically does not cause perforation even when the tip touches the intestinal wall. Since the tip can be placed in contact with the wall providing stability while dissection progresses, the procedure is technically easy and the efficacy is high. Moreover, the metal disc at the back of the insulated tip and the long arm extending from the disc hold and stabilize the tissue. In addition, the contact area between the tip and the tissue to be dissected is wide, allowing speedy treatment. The insulated tip also further ensures safety. Hence the IT knife nano is a very useful device.

Compared to the ITknife 2 used in gastric ESD, the IT knife nano used in the present study has a very small disc at the back of the insulated tip and is therefore suitable for use in organs with thin walls such as the large intestine. The data of the present study show that use of the IT knife nano shortens the treatment time while maintaining a high level of safety. Moreover, the superior hemostatic capability of the IT knife nano is probably another factor

that contributes to shorten treatment time. According to the present data, the number of hemostatic clamp use in one procedure was significantly fewer when using the IT knife nano. When using the needle-tip type devices, pre-coagulation of the vessels is necessary. With IT knife nano, the high hemostatic capability results in little bleeding during vessel dissection and reduced frequency of requiring pre- coagulation. This merit is probably attributed to the morphology of this device.

On the other hand, the IT knife nano is difficult to use when the submucosal space is small due to fibrosis or in bending locations. When there is no space due to fibrosis, the tip cannot hold on to the submucosa making dissection difficult. In the present study, we examined only large lesions, and they were mainly granular laterally spreading tumors (LST-G). Since there were few LST-NG that tend to develop fibrosis, the efficacy for this type of tumor is not known. In addition, use of the IT knife nano in bending locations is limited, because of the difficulty in executing left- right manipulations. When the present treatment results were compared between rectal and colonic lesions, equal efficacy was observed although the device was especially effective in the rectum, ascending colon and descending colon where there are few bends.

A limitation of the present study is that the data were obtained from a single facility, and bias related to the learning curve of the endoscopic technique cannot be excluded. However, the ESD were conducted by operators who were adequately experienced in gastric and esophageal ESD and had performed many cases of colorectal ESD. Therefore technical competence probably had little effect on the results. Moreover, the analysis was performed after 150 colorectal ESD had been performed, and the treatment time did not change significantly in subsequent cases. These facts also indicate that the effect of technical learning curve is minimal.

Although colorectal ESD has been standardized, future development should aim for safe and speedy treatment of large lesions. In this respect, the IT knife nano allows safe and speedy colorectal ESD.

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