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# **Per Anal Endoscopic Myectomy (PAEM) for rectal lesions with severe fibrosis and exhibiting the muscle-retracting sign**

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## **<Abstract>**

Background and study aims: Although endoscopic submucosal dissection has enabled complete tumor resection and accurate pathological assessments that are less invasive than surgery, the complete resection of lesions with severe fibrosis in the submucosal layer and exhibiting the muscle-retracting (MR) sign is often difficult. We devised a new method called 'Per Anal Endoscopic Myectomy (PAEM)' for rectal lesions with severe fibrosis, for which dissection is performed between the inner circular and outer longitudinal muscles, and examined its usefulness and safety.

Patients and methods: Cases that underwent PAEM in our hospital and affiliated hospitals were retrospectively reviewed.

Results: Ten rectal lesions were treated with PAEM between July 2015 and June 2017. *En bloc* resection with a negative vertical margin was achieved in 8 cases (80%) including two mucosal, one shallow submucosal, 4 deep submucosal, and one muscle-invasive lesion. Clinical courses in all cases after PAEM were preferable. In additional surgical cases, anus preservation was achieved based on the pathological results of PAEM.

Conclusions: PAEM for lesions with severe fibrosis exhibiting the MR sign would be safe and useful.

## **<Introduction>**

The technique of endoscopic submucosal dissection has recently been improved, and large and complex lesions may be resected *en bloc* [1-4]. Since rectal ESD is not limited by lesion size, it is possible to avoid invasive surgery and stoma and ensure a functional prognosis [5]. However, the complete resection of lesions with severe fibrosis in the submucosal layer and exhibiting the muscle-retracting (MR) sign, which is an interesting feature that the muscle layer under the tumor appears to be drawn by the neoplasm exhibited in some colorectal neoplastic lesions, is often difficult [6]. We devised a new method called 'Per Anal Endoscopic Myectomy (PAEM)' for rectal lesions with severe fibrosis, for which dissection is performed between the inner circular and outer longitudinal muscles instead of between the submucosal and muscle layers [7]. Several lesions have been resected to date using this method. This study aimed to examine the usefulness and safety of PAEM.

## **<Patients and methods>**

### **Patients**

Cases that underwent PAEM in our hospital and affiliated hospitals were retrospectively reviewed.

Indications for colorectal ESD were defined according to the colorectal ESD/EMR guidelines issued by the Japan Gastroenterological Endoscopy Society, in which carcinomas with only shallow T1(sm) invasion were examined [8]. However, assessing the depth of tumor invasion preoperatively is sometimes difficult, even with magnified surface observations and endoscopic ultrasound sonography, and the overestimation of tumor depth may result in unnecessary invasive surgery and stoma. Therefore, treatment options were carefully selected including the purpose of diagnostic ESD with informed consent.

### **PAEM procedure**

When ESD was performed for protruded lesions and fibrosis in the submucosal layer was suspected, pocket creation method (PCM) [9] was initially applied, and if severe fibrosis with the MR sign was found, PAEM was performed by an experienced operator. In PAEM, after circumferentially dissecting around the fibrotic area, the inner circular muscle was cut in a circular manner, which made the outer longitudinal muscle clearly visible [7]. We cleaned the muscle surface to make their fiber running easily viewable but didn't inject solution between the inner circular and outer longitudinal muscles because injecting in this space seemed difficult and fluid leak outside muscles was concerned. Instead, the space between these muscles was sparse and suitable traction with the tunneling method facilitated the dissection of this space. Flush knife-BT and BTS (FUJIFILM, Tokyo, Japan) were used with the Endo Cut or Dry Cut mode of ERBE VIO 300D for myotomy and muscle dissection.

When selective muscle dissection was difficult due to strong muscle retraction, full-thickness muscle dissection was partially performed.

If the bleeding occurred during the procedure, hemostasis was performed using Flush knife and/or hemostatic forceps.

Clip closure was not conducted after the procedure in most cases, except for those that resulted in full-thickness myectomy.

Peri-procedural antibiotics was administered for 3 days in all patients.

## **<Results>**

Ten rectal lesions were treated with PAEM between July 2015 and June 2017. Most lesions were located in the lower rectum and the main morphology was protruded type. Although the tumor depth was estimated to be deeper than T1b in some cases (Table 1), due to the possibility of overestimation, surgical invasiveness with patients' desire for diagnostic endoscopic treatment, and patients' refusal of surgery, PAEM was attempted.

Representative endoscopic and pathological images of PAEM are shown in Figures 1 and supplementary figures (Case no.6), while the outcomes of PAEM are shown in Table 1. The PAEM procedure is shown with a video clip (Case no.3).

Full-thickness muscle dissection was performed for two cases. The mean procedure time and the time spent for muscle dissection were 145.5 minutes (range: 39-450), and 15.5 (range: 3-34) respectively. There was no conspicuous complication.

*En bloc* resection with a negative vertical margin was achieved in 8 cases (80%), including two cases with mucosal invasion, one with shallow submucosal invasion, 4 with deep submucosal invasion, and one with muscle invasion. A positive horizontal margin in a non-fibrotic area was

observed in a mucosal lesion case due to unintentional procedural cutting. The other 2 cases showed tumor invasion to the muscle layer and the vertical margin was also positive. Clinical courses in all cases after PAEM were preferable, and the median hospitalization days was 7 (range 6-10), almost as same as usual ESD cases. There were no post-procedural complications such as delayed bleeding and perirectal absces. Three cases of resection with a negative margin, but with lymphovascular invasion of the tumor underwent additional surgery or adjuvant chemoradiation. In surgical cases, anus preservation was achieved. One of these cases underwent partial intersphincteric resection, which offers more preferable defecatory function after surgery than total intersphincteric resection, because the pathological result of PAEM showed mucosal dysplasia in the anal side component of the tumor. Two cases showing positive vertical margins due to muscle invasion underwent additional surgery; one had lymph node metastasis, but no local remnant tumor, while the other had tumor invasion to the subserosal layer and lymph node metastasis. Additional surgery has been performed for one case showing deep submucosal invasion, and lymph node metastasis (N1) without local remnant tumor was found.

## **<Discussion>**

The present study showed that lesions with severe fibrosis exhibiting the MR sign could be resected safely and completely with a high probability by PAEM.

When the MR sign is present, there are 2 general possibilities: the tumor has infiltrated the deep submucosa showing a desmoplastic reaction or only fibrosis created by peristalsis is present. One method for achieving R0 resection under these conditions is PCM [9]. It utilizes

traction in the fibrotic area and enables precise dissection above muscle fibers using the ESD technique. However, in the case of deep invasion, the risks of a positive vertical margin and overlooking lymphovascular invasion exist.

The ESD technique is also applied to various endoscopic procedures including muscular propria dissection, as exhibited by peroral endoscopic myotomy (POEM) and submucosal endoscopic tumor resection (SET) [10-12] .

Issues encountered in cases showing a positive MR sign, as discussed above, and experience of muscle dissection have led to the idea for and development of PAEM.

The best indication for PAEM may be a positive MR sign from only fibrosis, which requires complete endoscopic resection. Other cases may be those of deep submucosal tumor invasion without other high-risk factors, which are associated with a low risk of lymph node metastasis [13]. Under these conditions, PAEM contributes to the accurate diagnosis of tumor depths.

However, there is currently no modality with the ability to establish whether the MR sign is due to tumor invasion or only fibrosis. Therefore, PAEM may be considered when the MR sign is positive; however, surgery must be the first choice for suspected advanced cancer.

Another issue may be the detection of tumor invasion to the outer longitudinal muscle after PAEM has been started because the space between the inner and outer muscles cannot be observed. Although this is a rare condition because endoscopic treatment is not attempted when T2 cancer is suspected, when encountered, full-thickness muscle resection with PAEM is feasible; however, further investigations are needed; and endoscopic treatment may be suspended in favor of surgery because there could be theoretical risk of cancer cell seeding through the cut tumor vessels. If a patient is confirmed to have high-risk factors other than SM



deep invasion, additional therapies such as surgery and chemoradiation need to be considered.

The distal rectal lesions also can be managed by the surgical transanal excision.

Representative options is transanal endoscopic microsurgery (TEM). TEM is reported to achieve a high R0 resection rate by full-thickness fashion, and significantly reduce the need for further abdominal treatment [14]. Nevertheless, its indication for early rectal adenocarcinoma is usually limited to small lesions (< 4 cm). On the other hand, PAEM is on the extension of ESD, and large even circumferential resection is possible using ESD technique and PAEM only for area where MR sign is seen. Moreover, equipment for PAEM is as same as ESD, and it can be applied after MR sign confirmation during ESD, which seems to be a benefit compared to TEMS.

No complications developed in our PAEM cases. However, there exists a risk of pelvic sepsis as shown in a report on TEM, which mentioned its frequency as 3% [14].

We are administrating antibiotics for perioperative days, which may contribute to lowering the risk of infection. However, to guarantee further safety, clipping of the defected muscle area might be considered for all cases. Enough attention and measurement are also needed to avoid severe infection and quickly correspond to unfavorable situation when it occurs.

The limitation of this study includes the small number of cases treated by one experienced endoscopist. Further investigations with other endoscopists are warranted, as are further discussions on the value of PAEM in clinical practice.

However, we consider this technique to contribute to *en bloc* complete resection and accurate pathological diagnoses. Furthermore, even if additional surgery is required, based on accurate

histological assessments by PAEM, the extension of surgical resection may be reduced, thereby preserving anal function as much as possible. Although the number of cases encountered is still low, if the indication is limited to the lower rectum, PAEM will be performed safely.

In conclusion, PAEM for lesions exhibiting the MR sign with severe fibrosis would be safe and useful.

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## Conflict of Interests;

Dr. Toyonaga invented the Flush knife-BT and Flush knife-BTS in conjunction with Fujifilm and receives royalties from its sale.

## Figures/Tables

**Table 1 Characteristics of the lesions and Outcome of the PAEM**

no	location	Estimated tumor depth	Muscle dissection level	Major axis diameter of resected specimen (mm)	Major axis diameter of tumor (mm)	Histology of tumor	Lymphovascular invasion /Budding	Depth of tumor	R0 resection	Additional treatment
1	Rb	T1a	full thickness	75	55	tub1>tub2	v0, ly+	deeper than T2	R1 (VM)	surgery
2	Rb	T1b	selective	41	26	tub1	v1,ly0	T1b (4350 $\mu$ m)	R0	chemoradiation
3	Rb	T1b	selective	93	89	tub1	v1,ly0 budding G2	T2	R0	surgery
4	Rb	Tis, T1a	full thickness	66	50	tub1 with adenoma	v0,ly0	T1b (3500 $\mu$ m)	R0	observation
5	Rb	T1b	selective	37	24	tub 2 with adenoma	v2, ly0	T1b (4200 $\mu$ m)	R0	surgery
6	Rb	Tis, T1a	selective	60	50	tub 1 with adenoma	v0,ly0	T1b (1000 $\mu$ m)	R0	-
7	Rb	Tis	selective	135	135	tub1>pap>tub2	v0,ly0	Tis	R1 (HM)	observation
8	Rb	T1b	selective	122	113	tub 1 with adenoma	v1,ly1	T2	R1 (VM)	surgery
9	Rb	T1b	selective	74	61	pap>tub1 with adenoma	v0,ly0	Tis	R0	-
10	Ra-b	T1a	selective	165	162	tub1>pap>muc with adenoma	v0,ly0	T1b (7500 $\mu$ m)	R0	surgery

tub1, well-differentiated adenocarcinoma.

tub2, moderately differentiated adenocarcinoma.

pap, papillary adenocarcinoma.

muc, mucinous adenocarcinoma.

VM, vertical margin.

HM, horizontal margin.

## Figure 1

- A) Myotomy of the inner circular muscle and dissection between the inner circular and outer longitudinal muscles.
- B) Pathological image of the lesion removed with the internal circular muscle. The pathological result was tub 1 with adenoma, specimen size 60x60 mm, tumor size 50x50 mm, pT1b(SM;1000µm), ly0 (D2-40), v0 (EVG), budding (G1), pHM0, pVM0.

## Supplemetary Figures

- A) Is lesion in the lower rectum.
- B) Indigo carmine staining view.
- C) The procedure was started with pocket creation method.
- D) The muscle-retracting sign found at the center of the lesion.
- E) PAEM was performed.
- F) Myotomy of the inner circular muscle.
- G) H) I) Dissection between the inner circular and outer longitudinal muscles.
- J ) Dissection between the muscles has been completed.
- K) The artificial ulcer left after PAEM.
- L) Macroscopic view of the resected specimen from the submucosal side accompanying the internal circular muscle.
- M) Macroscopic view of the resected specimen from the mucosal side.
- N) Pathological image of the lesion removed with the internal circular muscle. The pathological result was tub 1 with adenoma, specimen size 60x60 mm, tumor size 50x50 mm, pT1b(SM;1000µm), ly0 (D2-40), v0 (EVG), budding (G1), pHM0, pVM0.