Original Article

Endoscopic Mucosal Resection (EMR) for Colorectal Lesions and Lesion-lifted Condition as an Indicator of the Tumor Invasion

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Abstract

Utility and safety of EMR for colorectal lesions and lesion-lifted condition as an indicator of the tumor invasion were investigated. We investigated 672 cases and 708 lesions treated between 1993 and 2006. We classified the lesion-lifted condition at the time of submucosal fluid injection, using four categories: "completely lifted/soft", "completely lifted/hard", "incompletely lifted", and "non-lifting". The pit patterns and lifted conditions were related to tumor pathology and the extent of tumor invasion, and often corresponded to particular macroscopic types of tumors. Early colorectal cancer was treated in 231 cases by EMR alone, while 29 cases received additional colectomy after EMR because of an unfavorable pathology. Complications after EMR included bleeding in 19 cases (2.8%) and abdominal pain in 3 (0.4%). There were no cases of perforation. Recurrence occurred in 5 cases (2.2%) (4 cases were cured by re-EMR; one case required surgical resection) out of 231 cancer cases.

The classification of the lesions according to their lifted condition and pit pattern was useful to determine whether EMR was indicated. Furthermore, EMR is very safe methods because of the scarcity of complications, and they provide a success rate of about 98% for the treatment of early colorectal cancer.

Keywords: endoscopic mucosal resection (EMR), lesion-lifted condition, colorectal neoplasm, non-lifting sign, pit pattern

(Received March 24, 2008; Accepted March 29, 2008)

Introduction

EMR is a less invasive treatment option for colorectal lesions, and it offers the additional benefit of providing specimens for histologic analysis. It was first described by Deyle et al. in 1973 as a strip biopsy technique¹⁾, and it was used in the treatment of gastric cancer by Tada et al. in the 1980s²⁾. In the 1990s, it came into use for the treatment of colorectal lesions. EMR is a local treatment, so its selection as an endoscopic treatment for early colorectal cancer depends on the diagnosed depth of tumor invasion. This is because the complete cure of colorectal cancer by EMR treatment requires not only negative resection margins to ensure the success of local treatment, but also an absence of possible lymph node metastasis and distant metastases. The risk of lymph node metastasis is mainly related to the depth to which the cancer invades the intestinal wall. Mucosal cancers and minimally invasive submucosal cancers, for example, are seldom accompanied by lymph node metastases³⁾.

The lifted condition is the degree to which a lesion is lifted after submucosal injection, and in 2001 we classi-

fied it into four categories⁴⁾. Because this classification has proven useful for estimating the depth of tumor invasion, we are now going to describe our EMR technique, methods of diagnosing the depth of invasion, including the pit pattern and the lifted condition and clinical course after EMR.

Patients and methods

We investigated 672 cases and 708 colorectal lesions treated between 1993 and 2006. We used EMR to treat colorectal adenoma in 375 lesions, cancer with adenoma in 107, mucosal cancer in 97, submucosal cancer in 78, and other conditions in 51. Before we performed EMR, we observed the pit pattern under indigo carmine dye spray, if possible, with a magnifying endoscope. And also Kudo's classification of pit pattern was used (Fig. 1). We classified each lesion according to its lifted condition after submucosal liquid injection, using four categories: "completely lifted/soft (CLS)", "completely lifted/hard (CLH)", "incompletely lifted (ICL)" and "non-lifting (NL)" (Fig. 2). A CLS lesion is completely lifted by submucosal injection, and it stretches softly into a dome. A CLH lesion is completely lifted, but it is rigid and maintains its original form. An ICL lesion is slightly lifted, but the surrounding mucosa lifts higher than the lesion. An NL lesion is not lifted, and only the surrounding mu-

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cosa is elevated (Fig. 3).

Orthodox EMR is performed as shown in Fig. 4. After observation of the lesion, hypersaline solution with epinephrine is injected into the submucosal layer. We observe the lifted condition at this time. Then we capture a bulging lesion in a surgical snare and remove it by cauterizing with a high-frequency current. Finally

it is brought out with tripod forceps. Some particularly difficult lesions can not be captured by an ordinary soft snare, but in these cases we have found that a spiral snare works well because of the increased stiffness of the spiral-wound wire. Another version of the EMR technique is known as EMR with transparent cap. In this procedure, we begin by widening a soft snare inside a trans-

Fig. 1 Classification of the pit pattern by Kudo

Kato H et al: (2001) Endoscopy 33: 568-573.

Fig. 2 Classification of the lesion-lifted condition

parent cap and suctioning a lesion into the cap. Once the lesion is sucked in through the snare, the snare is tightened around it. After we inflate the lumen again for the good endoscopic view and confirm that the snare has not captured any of the muscularis propria, we cauterize and remove the lesion. For large lesions, we perform fractional excision; we call this technique in particular

EPMR (endoscopic piece meal resection).

We performed analysis on the lesions' lifted conditions, endoscopic findings (including pit patterns), pathological findings, and clinical courses of our EMR cases. The statistical analysis was performed with a chi square test; a p value of <0.05 was considered statistically significant.

Fig. 3 Endoscopic view in each of the lesion-lifted condition

Fig. 4 Orthodox method of EMR

Results

The relationship between a lesion's lifted condition and its macroscopic type is shown in Table 1. Type IIa was found to predominate among CLS lesions, while elevated lesions like type Ip, Isp, and Is tended to fall into the CLH category. By contrast, type IIa+IIc was the most common type of morphology among ICL and NL lesions. The relationships between lifted conditions from CLS to ICL lesions, and their corresponding macroscopic types were statistically significant. But when we compared ICL and NL lesions, there were no relations between the lifted conditions and the macroscopic types. The mean size of lesions in each lifted-condition category is shown in Fig. 4. The mean size of tumors was about 15 mm in diameter in every lifted-condition category.

The relationship between a lesion's lifted condition and its pit pattern is shown in Table 2. Many of the lesions displaying a IIIL pit pattern were classified as CLS, while many lesions displaying a V pit pattern were classified as ICL or NL. Of the lesions displaying a type V or IIIs pit, most of the ICL lesions and all of the NL lesions were sm massive invading lesions.

The relationship between a lesion's lifted condition and the depth of invasion is shown in Table 3. All CLS lesions were found to be sm1 or shallower, while the CLH category included 15 sm2 and 7 sm3 lesions. The rate of sm massive cancer in CLH lesions was 10.4%. ICL lesions ranged from sm1 to sm3, and almost all of the NL lesions showed invasion to sm3 or deeper. In three cases, NL lesions were adenomas that had previously been subjected to a deep biopsy.

In 21 cases, indicated by parentheses in Table 3, we were not able to perform EMR because of an unfavorable lifted condition. In 29 cases out of 651 cases performed EMR actually, the patients required additional surgery due to unfavorable pathology. The rate of fractional excision increased with lesion size. Lesions larger than 30 mm were excised by EPMR in 68.4% of patients.

The lifted condition of the lesions affected the success rate of the treatment: treatment with EMR or EPMR alone was very often successful in CLS and CLH cases, but the same treatment was successful in only 57% of ICL cases and only 25% of NL cases (Fig. 5). Some complications occurred, as shown in Table 4: bleeding that required endoscopic hemostasis was present in 1.6%, and excision of the muscularis propria layer occurred in 4 cases, but both perforation and massive bleeding requiring surgery were totally absent.

There were mucosal recurrences in 4 cases. All of them were initially resected using the EPMR technique, but we were able to remove all of the recurrence lesions with repeated endoscopic resection. Only one case recurred in the same local area and liver, 3 years after the

initial EPMR. This patient received surgery. The results we obtained using EMR and EPMR for early colorectal cancer are summarized in Fig. 6. Patients were cured without recurrence in 97.8% of the 231 colorectal cancer cases with which we followed up for 6.1 years (mean) after performing EMR or EPMR (Fig. 7).

Discussion

Massive submucosal invasion, vascular invasion, poorly differentiated adenocarcinoma, and positive margins have been mentioned as risk factors for recurrence after endoscopic treatment⁵⁾. The depth of invasion into the wall is particularly important, and its effect has been studied intensively⁶⁾. Most researchers agree that 10 to 20% of submucosal colorectal cancers are accompanied by lymph node metastasis⁶⁾. Kudo⁷⁾ divided the submucosal layer into three layers – sm1, sm2, and sm3 – and subclassified sm1 cancer as sm1a, sm1b, sm1c depending on the size of the lesion. In this classification, sm1a cancers are not associated with lymph node metastasis. This is one reason why it is important to diagnose the depth of the lesions prior to endoscopic treatment: it can help predict the presence of lymph node metastasis.

There are several ways to diagnose the depth of invasion in colorectal neoplasm. Endoscopic ultrasonography (EUS) is a highly accurate method of measuring the depth of invasion⁸⁾, but it requires a special apparatus as well as knowledge of the correct technique. Another method of diagnosis is to confirm special findings in colonoscopy. Special findings such as depression, ulceration, fold convergence, bleeding tendency, irregularly shaped, and a non-lifting sign indicate a deep invasion^{9, 10)}. The “non-lifting sign” is a simple yes/no classification, and, compared to EUS, it is a much easier way to determine whether EMR is indicated. However, since it is by no means rare for submucosal invasion to be found among lesions that show a negative lifting sign, we have created a more detailed classification of lifting conditions. In a previous study, we focused on the tumor's lifting condition after submucosal injection and classified it into four types⁴⁾. This classification is closely related to the depth of invasion, and has proved to be particularly useful in the identification of early colorectal cancers that are good candidates for endoscopic treatment, without requiring any special apparatus.

We observed a close relationship between a lesion's lifted condition and the associated tumor's morphological classification. Flat types of tumors, such as type IIa, were found to predominate among CLS lesions, while elevated tumors like types Ip, Isp and Is were most common among CLH lesions. We think that the flat type tended to fall into the CLS category because flat tumors are more easily stretched than elevated tumors. Lesions showing depressions, such as type IIa+IIc, were hard to

Table 1. Relationship between the lifted condition and the macroscopic type

	Ip	Isp	Is	Ila	Ilc	Ila+Ilc	
CLS	0	17	51	328	29	3	**
CLH	9	39	72	70	13	9	
ICL	0	9	12	21	7	7	*
NL	0	0	4	2	1	5	

** P<0.001 * P<0.05

Table 2. Relationship between the lifted condition and the pit pattern (No. of lesions)

	I	II	IIIL	IIIs	IV	V	
CLS	2	35	239	117	33	2	**
CLH	13	0	71	72 (6)	29	27 (9)	
ICL	2	0	13	9 (6)	2	30 (22)	**
NL	0	0	2	2 (2)	1	7 (7)	

(): sm massive = sm2~ ** P<0.001

Table 3. Relationship between lifted condition and depth of invasion (No. of lesions)

	nc	cia	m	sm1	sm2	sm3 ~	
CLS	322	60	43	3	0	0	***
CLH	88	41	49	12	15	7	
ICL	13	6	5 (2)	4	12 (2)	16 (9)	**
NL	3	0	0	0	0	9 (8)	

nc=non cancer, cia=Cancer in adenoma *** P<0.001

(): cases that were not performed EMR

Table 4. Complications

	Cases
Bleeding (endoscopic Tx)	11 (1.6%)
Bleeding (conservative Tx)	8 (1.2%)
Abdominal pain	3 (0.4%)
Excision of the mp layer	4 (0.6%)
Perforation	0

Fig. 5 Mean size every lifted condition of the lesion tried EMR

Fig. 6 Success rate of only endoscopic treatment

Fig. 7 Outcome of EMR (including EPMP) for early colorectal cancer

be lifted; they were generally associated with deep invasion, so it is particularly necessary to use caution in the case of depressed lesions. The size of a tumor, on the other hand, does not necessarily correspond to the associated lesion's lifted condition. This implies that the factor for carcinoma staging is the depth of invasion, but not the size of the lesion. Large and deeply invaded tumors are not suitable for endoscopic treatment, but mucosal tumors are good candidates for EMR regardless of their size.

Pit patterns in the large intestine were classified into 7 types by Kudo¹¹⁾. He observed that small round pit patterns (type IIIs) and non-pit patterns (type V) were common in depressed lesions, and that these depressed lesions had invaded the deeper layers more rapidly than protruding lesions. Our data indicated that many ICL and NL lesions displayed a type V pit pattern, and also that most of the ICL lesions and all of the NL lesions displaying a type V or IIIs were sm massive invading lesions. Thus we can predict the depth of invasion to some extent by observing a lesion's pit pattern and lifted condition. Kobayashi et al. described that, because of its lower sensitivity and accuracy, the non-lifting sign will not replace endoscopic assessment, and that, if a lesion does not lift, this can make resection technically difficult, but it does not reliably predict deeper cancerous invasion¹²⁾. Yet according to those authors' own data, the non-lifting sign predicted sm massive invasion with an accuracy of 94.8%, which is not too low to be useful. We believe that classifying a lesion's lifted condition and observing its pit pattern are useful aids in deciding whether EMR is indicated, especially because a lesion's lifted condition often affects the success of endoscopic treatments. It is also important to know the sm massive invading rate associated with each of the lifted conditions.

There were no severe complications in the course of EMR and EPMR, so these endoscopic treatments may be considered completely safe. As far as clinical course is concerned, we experienced only 4 mucosal recurrences and one local and hepatic recurrence after EPMR not EMR. Indeed, the specimens resected by EPMR are said to be difficult to be reconstructed pathologically. But, 4 mucosal recurrent cases healed by repeated endoscopic resection. Currently, a new method of endoscopic submucosal dissection (ESD) for the en-bloc excision of large lesions is coming into use, so it is becoming easier to correctly diagnose the pathology of resected lesions¹³⁾. The risk of perforation, however, is very high with this new technique, so the decision to use it must be made carefully.

Observations of pit patterns and lifted conditions can help us determine therapeutic strategies for our patients: lesions displaying type I to type IV pit patterns may be cured by endoscopic polypectomy or EMR; when lesions display type V pit patterns, it is necessary to observe the

lifted condition to determine whether EMR is an appropriate treatment. When the lifted condition of a lesion is CLS or CLH, it is a good indication that EMR will be successful. When the lifted condition is ICL, however, EMR has a smaller chance of success. If an unfavorable pathology is recognized after EMR, surgical resection such as a laparoscopic colectomy is recommended.

Conclusions

Classification of the lifted conditions and observation of the pit patterns of lesions were useful to determine whether EMR was indicated. EMR provided a success rate of about 98% for the treatment of early colorectal cancer, and caused few complications. In EPMR, follow-up colonoscopy is important because a mucosal recurrence often occurs; this can be cured by repeated EMR.

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