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BRIEF ARTICLES

Meta-analysis and systematic review of colorectal endoscopic mucosal resection

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Abstract

AIM: To evaluate the proportion of successful complete cure *en-bloc* resections of large colorectal polyps achieved by endoscopic mucosal resection (EMR).

METHODS: Studies using the EMR technique to resect large colorectal polyps were selected. Successful complete cure *en-bloc* resection was defined as one piece margin-free polyp resection. Articles were searched for in Medline, Pubmed, and the Cochrane Control Trial Registry, among other sources.

RESULTS: An initial search identified 2620 reference articles, from which 429 relevant articles were selected and reviewed. Data was extracted from 25 studies (n = 5221) which met the inclusion criteria. All the studies used snares to perform EMR. Pooled proportion of *en-bloc* resections using a random effect model was 62.85% (95% CI: 51.50-73.52). The pooled proportion for complete cure *en-bloc* resections using a random effect model was 58.66% (95% CI: 47.14-69.71). With higher patient load (> 200 patients), this complete cure *en-bloc* resection rate improves from 44.19% (95% CI: 24.31-65.09) to 69.17% (95% CI: 51.11-84.61).

CONCLUSION: EMR is an effective technique for the resection of large colorectal polyps and offers an alternative to surgery.

INTRODUCTION

The use of endoscopic mucosal resection (EMR), pioneered in Japan for the treatment of early gastric cancer, has expanded to include therapy of other early gastrointestinal malignancies and pre-cancerous lesions such as adenomas. At the same time, this technique has gained acceptance in Europe and in the US, especially for the treatment of Barrett's esophagus with high grade dysplasia[1-3]. Several variations of the EMR technique have been devised such as inject-lift-cut, strip biopsy, suction cup (EMRC), and EMR with a ligating device.

Throughout the world, adenomas of the colorectum represent the single most important premalignant lesion of the GI tract. Large (> 2 cm) colorectal polyps have been found in 0.8%-5.2% of patients undergoing colonoscopies for different indications[4].

Large sessile and flat polyps represent a major technical challenge to conventional snare resection. Additional procedures and therapies such as Argon plasma coagulation are frequently needed to destroy remnant tissue after resection[5]. When these techniques are not used or possible, patients are frequently referred for surgical resection[6].

EMR has been shown to be useful in the removal of large colorectal sessile and flat lesions[7]. However, there are limits to the size of lesions which can be removed *en-bloc* with the various EMR techniques, with 1.5-2 cm generally being the upper limit[8].

En-bloc removal of large polyps is desirable as it facilitates thorough histological evaluation related to the

completeness of resection, and is associated with a lower recurrence rate as compared to piecemeal removal[9-14].

MATERIALS AND METHODS

Study selection criteria

Studies using EMR technique to resect large (> 2 cm) colorectal polyps were selected. Successful cure *en-bloc* resection was defined as one piece removal with tumor-free vertical and lateral margins.

Data collection and extraction

Articles were searched for in Medline, Pubmed, Ovid journals, Japanese language literature, Cumulative Index for Nursing & Allied Health Literature, ACP journal club, DARE, International Pharmaceutical Abstracts, old Medline, Medline non-indexed citations, OVID Healthstar, and the Cochrane Controlled Trials Registry. The search terms used were EMR, endoscopic mucosal resection, colon polyps, lateral spreading tumors, large polyps, nonpolypoid colon lesions, flat colon polyps, and flat adenomas. Two authors (SP and YK) independently searched and extracted the data for revising into an abstracted form. Any differences were resolved by mutual agreement.

Quality of studies

Clinical trials with a control arm can be assessed for the quality of the study. A number of criteria have been used to assess the quality of a study (e.g. randomization, selection bias of the arms in the study, concealment of allocation, and blinding of outcome)[15,16]. There is no consensus regarding how to assess studies without a control arm. Hence, these criteria do not apply to studies without a control arm[16]. Therefore, for this meta-analysis and systematic review, studies were selected based on completeness of data and inclusion criteria.

Statistical methods

This meta-analysis was performed by calculating pooled proportions, i.e. pooled proportion of *en-bloc* resections and complete cure *en-bloc* resections. Firstly, the individual study proportions of successful resections were transformed into a quantity using Freeman-Tukey variant of the arcsine square root transformed proportion. The pooled proportion was calculated as the back-transform of the weighted mean of the transformed proportions, using inverse arcsine variance weights for the fixed effects model and DerSimonian-Laird weights for the random effects model[17,18]. Forrest plots were drawn to show the point estimates in each study in relation to the summary pooled estimate. The width of the point estimates in the Forrest plots indicated the assigned weight to that study. The heterogeneity among studies was tested using Cochran's Q test based upon inverse variance weights[19]. If P value was > 0.10, the null hypothesis was rejected that the studies were heterogeneous. The effects of publication and selection bias on the summary estimates were tested by Begg-Mazumdar bias indicator[20]. Also, funnel plots were constructed to evaluate potential publication bias using the standard error and diagnostic odds ratio[21,22].

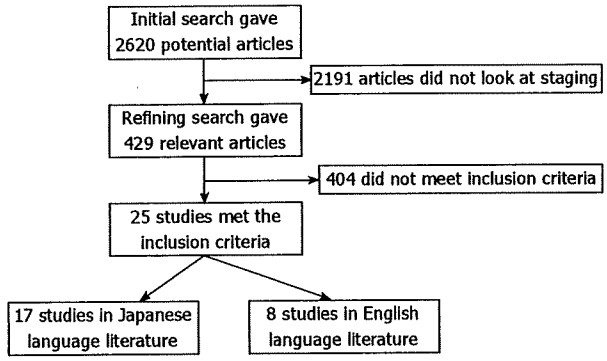

Figure 1 Search results.

RESULTS

An initial search identified 2620 reference articles from which 429 relevant articles were selected and reviewed. Data was extracted from 25 studies (n = 5221) which met the inclusion criteria[23-46]. The search results are shown in Figure 1. All the studies used snare to perform EMR. Two studies used a strip biopsy technique[42,43]. The mean size of the polyps was 22.48 ± 4.52 mm. There were 3755 successful *en-bloc* resections. The study characteristics are shown in Table 1.

The pooled proportion of *en-bloc* resections using a random effect model was 62.85% (95% CI: 51.50-73.52). Forest plot in Figure 2A depicts the individual study proportion of successful *en-bloc* resections in relation to the pooled estimate. The pooled proportion for complete cure *en-bloc* resections using a random effect model was 58.66% (95% CI: 47.14-69.71). Figure 2B shows Forrest plot depicting the individual study successful cure *en-bloc* resections in relation to the pooled estimate. The fixed effect model was not used because of the heterogeneity of studies.

Subgroup analysis was carried out by grouping studies according to the study population. This was done because the expertise needed to perform procedures might have affected the outcome. Studies were categorized into three groups: < 100 patients, 100-200 patients and > 200 patients. The proportions for successful *en-bloc* and successful cure *en-bloc* resections are shown in Table 2.

The publication bias calculated by Begg-Mazumdar bias indicator for successful cure *en-bloc* resections concluded that the Kendall's tau b value was -0.19 (P = 0.17). The funnel plot in Figure 3 shows that there was no publication bias for successful cure *en-bloc* resections.

DISCUSSION

Some colorectal cancers develop from adenomas. The risk of high grade dysplasia and cancer increases with the size of the lesion. Endoscopic removal of large (> 2 cm) sessile and flat polyps represents a difficult challenge for conventional snare resection and they are frequently managed by piecemeal resection or surgically[6,47]. EMR was the definitive procedure in all the collated studies. The data for complications was not available for the majority of the studies, so this data was not collected. EMR is a technique that can be applied to sessile and flat

	Author, yr	Instrument used	*n*	Type of polyp	Technique
1	Matsushita *et al*[23], 2003	Snare	935	No information	EMR
2	Imai *et al*[24], 1999	Snare	30	No information	EMR
3	Igarashi *et al*[25], 1999	Snare	884	No information	EMR
4	Oka *et al*[26], 2005	Snare	410	Lateral spreading tumor	EMR
5	Sano *et al*[27], 2004	Snare	392	Lateral spreading tumor	EMR
6	Hotta *et al*[28], 2003	Snare	284	Protrusion 68, flat 213, depressed 3	EMR
7	Matsuda *et al*[29], 2006	Snare	154	Is,Isp 33, LST-G 96, NG 25	EMR
8	Yasumoto *et al*[30], 2005	Snare	240	LST-G 180, NG 60	EMR
9	Terai *et al*[31], 2003	Snare	223	Lateral Spreading tumor	EMR
10	Nozaki *et al*[32], 2006	Snare	198	Ip 3, Isp 34, Is 7, LST-G 85, NG 28	EMR
11	Watari *et al*[33], 1998	Snare	186	Lateral spreading tumor	EMR
12	Sugisaka *et al*[34], 2003	Snare	162	No information	EMR
13	Matsunaga *et al*[35], 1999	Snare	134	No information	EMR
14	Nomura *et al*[36], 2001	Snare	54	No information	EMR
15	Kobayashi *et al*[37], 1999	Snare	131	No information	EMR
16	Nakajima *et al*[38], 2006	Snare	52	No information	EMR
17	Cho *et al*[39], 1999	Snare	34	No information	EMR
18	Saito *et al*[40], 2001	Snare	170	Lateral spreading tumor	EMR
19	Tanaka *et al*[13], 2001	Snare with needle spike	81	Lateral spreading tumor	EMR
20	Ahmad *et al*[41], 2002	Snare with suction	41	Colon and rectum	EMR
21	Hurlstone *et al*[42], 2004	Strip technique of Karita	80	Rectal villous adenoma	EMR
22	Hurlstone *et al*[43], 2005	Strip technique of Karita	62	Rectal villous adenoma	EMR
23	Su *et al*[44], 2005	Snare with needle spike	152	Colonic nonpolypoid lesions	EMR
24	Uraoka *et al*[45], 2005	Snare	113	Lateral spreading tumor	EMR
25	Kawamura *et al*[46], 1999	Snare	19	Submucosal invasive colorectal cancers	EMR

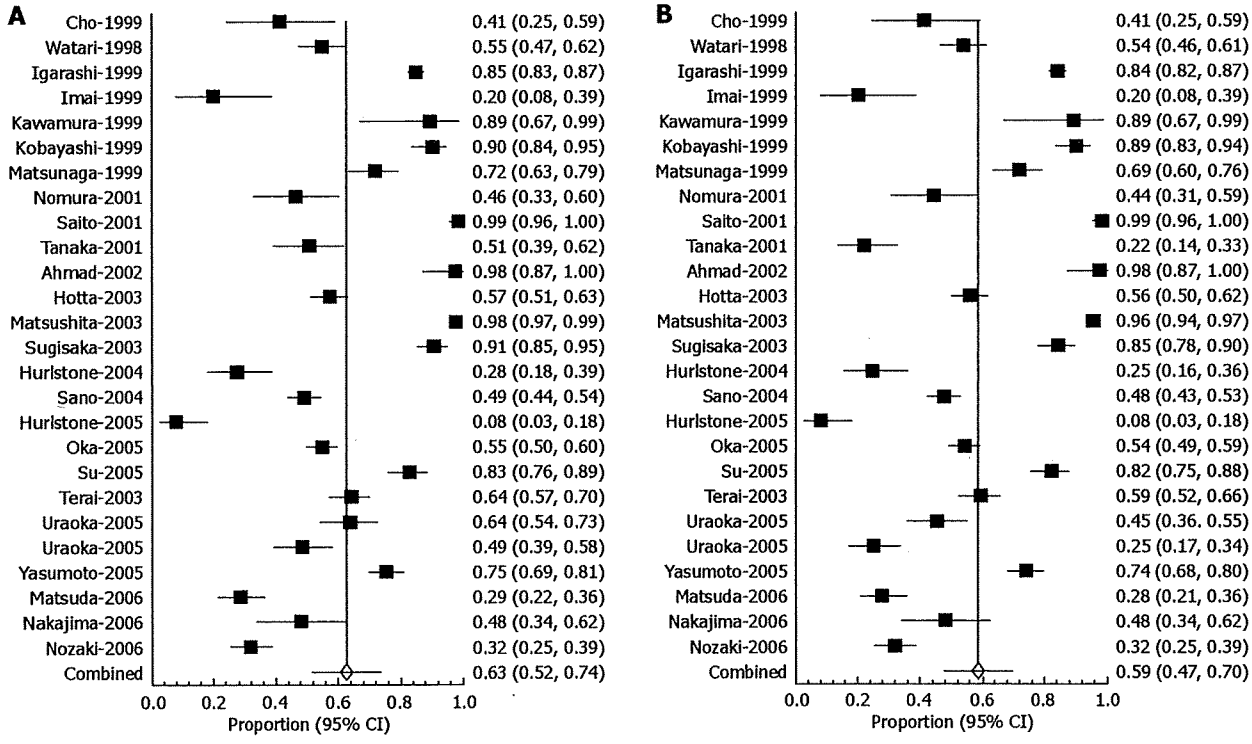

Figure 2 Forrest plot showing successful *en-bloc* (A) and cure *en-bloc* (B) resection.

lesions. Though initially used for the treatment of early gastric cancer in Japan, the technique has been expanded to the therapy of large colorectal neoplasms[7].

This meta-analysis revealed that *en-bloc* resection was achieved in 62.85% of lesions and tumor-free vertical and lateral margins were achieved in 58.6%. These results compare well to *en-bloc* resection rates achieved by conventional polypectomy snare, which have been reported to be between 7% and 34% for large sessile polyps[6,48].

Furthermore, our meta-analysis revealed that experience performing EMR plays an important role in achieving a better *en-bloc* resection and cure *en-bloc* tumor-free rate. Studies reporting more than 200 lesions removed reported a 71.39% *en-bloc* resection of lesions and tumor-free vertical and lateral margins in 69.17% of cases, while studies reporting less than a 100 lesions reported a

Table 2 Results based on study size

Study size	No. of studies	Successful *en-bloc* resection (95% CI)	Successful cure *en-bloc* resection (95% CI)
< 100 patients	9	48.07% (28.36-68.09)	44.19% (24.31-65.09)
100-200 patients	9	68.93% (50.39-84.76)	63.32% (43.50-81.04)
> 200 patients	7	71.39% (52.24-87.20)	69.17% (51.11-84.61)

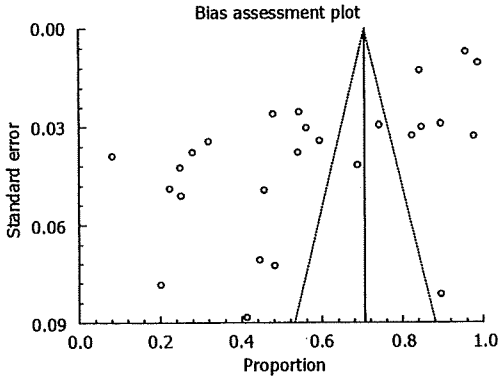

Figure 3 Funnel plot showing publication bias for successful cure *en-bloc* resection.

48.07% *en-bloc* removal and tumor-free vertical and lateral margins in 44.19% of cases. This indicates that experience in the technique of EMR increase the cure *en-bloc* rate.

In the present meta-analysis we searched the world literature which included articles published in Japanese language literature. We believe that our results are a reasonable reflection of the status of EMR in the therapy of large colorectal polyps.

EMR is an effective technique for resection of large colorectal polyps. The technique offers an alternative to surgery. This meta-analysis shows that the success rate for *en-bloc* margin-free resection is not high but improves with experience. Improvements in techniques and equipment are needed to increase complete cure *en-bloc* resection rates.

COMMENTS

Background

Endoscopic mucosal resection (EMR) has emerged as an alternative to surgery for the resection of large colorectal polyps. Complete cure with tumor-free lateral and vertical margins would prevent further therapy. Published data regarding successful *en-bloc* resection with tumor-free margins by EMR has been varied.

Innovations and breakthroughs

EMR has been shown to be useful in the removal of large colorectal sessile and flat lesions. However, there are limits to the size of lesions which can be removed *en-bloc* with the various EMR techniques, with 1.5-2 cm generally being the upper limit. *En-bloc* removal of large polyps is desirable as it facilitates thorough histological evaluation related to the completeness of resection, and is associated with a lower recurrence rate as compared to piecemeal removal.

Applications

EMR is an effective technique for resection of large colorectal polyps and offers an alternative to surgery. This meta-analysis shows that the success rate for *en-bloc* margin-free resection is not high but improves with experience. Improvements in techniques and equipment are needed to increase complete cure *en-bloc* resection.

Peer review

The authors evaluated the proportion of successful complete cure *en-bloc* resections of large colorectal polyps achieved by EMR. They found that EMR is an effective technique for resection of large colorectal polyps. This article is well written and easy to read.

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BRIEF ARTICLE

CO_2 insufflation for potentially difficult colonoscopies: Efficacy when used by less experienced colonoscopists

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Abstract

AIM: To clarify the effectiveness of CO_2 insufflation in potentially difficult colonoscopy cases, particularly in relation to the experience level of colonoscopists.

METHODS: One hundred twenty potentially difficult cases were included in this study, which involved females with a low body mass index and patients with earlier abdominal and/or pelvic open surgery or previously diagnosed left-side colon diverticulosis. Patients receiving colonoscopy examinations without sedation using a pediatric variable-stiffness colonoscope were divided into two groups based on either CO_2 or standard air insufflation. Both insufflation procedures were also evaluated according to the experience level of the respective colonoscopists who were divided into an experienced colonoscopist (EC) group and a less experienced colonoscopist (LEC) group. Study measurements included a 100-mm visual analogue scale (VAS) for patient pain during and after colonoscopy examinations, in addition to insertion to the cecum and withdrawal times.

RESULTS: Examination times did not differ, however, VAS scores in the CO_2 group were significantly better than in the air group ($P < 0.001$, two-way ANOVA) from immediately after the procedure and up to 2 h later. There were no significant differences between either insufflation method in the EC group ($P = 0.29$), however, VAS scores for CO_2 insufflation were significantly better than air insufflation in the LEC group ($P = 0.023$) immediately after colonoscopies and up to 4 h afterwards.

CONCLUSION: CO_2 insufflation reduced patient pain after colonoscopy in potentially difficult cases when performed by LECs.

Key words: CO_2 insufflation; Colonoscopy; Difficult colonoscopy; Experienced colonoscopist; Training

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INTRODUCTION

Colonoscopy has a high profile because of its increasingly important role in successfully preventing, detecting and treating colorectal cancer[1,2], however, some patients experience considerable abdominal pain and discomfort when the procedure is performed using air insufflation. In particular, the so-called "difficult colonoscopy" cases[3-6], which involve female patients with a relatively

low body mass index (BMI), patients with a history of abdominal and/or pelvic open surgery and male patients with diverticulosis, often require prolonged insertion to the cecum, thus this procedure can cause increased abdominal pain and discomfort for such patients.

Factors accounting for longer examination times and increased abdominal pain and discomfort can be derived from both a patient's condition and the examining colonoscopist's skill and experience[7-9]. Novice and even moderately skilled colonoscopists must improve their technical abilities by gaining experience in successfully handling difficult colonoscopies to become qualified experts, as a suitably high-level colonoscopy training environment has not been established as yet[10,11].

CO_2 insufflation has been reported to reduce patient abdominal pain and discomfort during and after colonoscopies[12-15]. Although the safety and efficacy of CO_2 insufflation during colonoscopies have been assessed in earlier studies, air insufflation is still the standard method due to a lack of suitable equipment and inadequate information as to when and on whom CO_2 insufflation should be used during colonoscopy examinations.

We decided to conduct a prospective randomized controlled trial to test the hypothesis that CO_2 insufflation reduces patient abdominal pain and discomfort during and after colonoscopy examinations in potentially difficult cases.

MATERIALS AND METHODS

Study protocol

Consecutive patients considered potentially difficult cases for colonoscopic intubation were included in this prospective randomized controlled trial which took place between September 2006 and October 2007. The aim of this study was to clarify the effectiveness of CO_2 insufflation during colonoscopy examinations, with the primary objectives of assessing both patient tolerance and the safety of CO_2 insufflation in these potentially difficult cases. A secondary objective was to clarify any differences between the two insufflation methods in relation to the experience level of the participating colonoscopists. This study was approved by the Ethics Committee at Okayama University Hospital.

Patients

Patients considered potentially difficult colonoscopy cases, based on published information and clinical experience, were selected, and included females with a relatively low BMI (BMI < 22), patients with a history of abdominal and/or pelvic open surgery, with the exception of low risk procedures for adhesions such as appendectomy or hernia repair, and male patients with previously diagnosed left-side diverticulosis[3-6].

The indications for colonoscopy examination were the standard clinical criteria: colorectal cancer screening, surveillance for polyps, a positive fecal occult blood test, abdominal symptoms or anemia. Exclusion factors included severe heart or lung disease, a prior colorectal resection, inflammatory bowel disease, severe hematochezia and repeat colonoscopy for therapeutic procedures including polypectomy.

Written informed consent was obtained from each patient and enrolled patients were randomly divided into two groups for colonoscopy examinations using either CO_2 or standard air insufflation. Group allocation for both patients and colonoscopists was performed by specially assigned nurses using standard randomization lists which contained consecutive patient numbers. Each number was linked to one of the two study groups for allocation purposes. These lists were not accessible by the participating colonoscopists.

Colonoscopy using CO_2 insufflation

Patients underwent bowel preparation with sodium picosulfate the day before their examinations and two liters of polyethylene glycol solution-containing lavage the morning of their colonoscopies. Scopolamine butylbromide (20 mg) was administered intramuscularly to suppress bowel movement, while patients with cardiac disease or benign prostatic hypertrophy received glucagon (1 IU) intramuscularly. Patients were not sedated, although midazolam (2-3 mg, iv) was administered based on the examining colonoscopist's judgment or when requested by the patient due to abdominal pain or distension. Examinations were performed using a pediatric variable-stiffness colonoscope (PVSC) with a distal tip diameter of 11.3 mm (PCF-Q260AI, Olympus Co, Tokyo, Japan).

Procedures were randomly performed by eight colonoscopists who had earlier been divided into two groups according to their colonoscopy experience: four highly experienced colonoscopists (EC) group each of whom had been in colonoscopy practice for over 10 years (TU, JK, KT and SH), and four less experienced colonoscopists (LEC) group with 5-7 years of colonoscopy practice during which each had performed 900-1500 colonoscopies (MK, SI, KH and HF).

If an examining colonoscopist from the LEC group failed to pass through the sigmoid-descending colon junction within 15 min or a patient complained of severe pain, a colonoscopist from the EC group replaced the initial examiner before midazolam was administered and continued insertion to the cecum. When such a case involved a colonoscopist from the EC group as the initial examiner, a more experienced member of the EC group would continue the procedure. After reaching the cecum, the initial examiner proceeded with withdrawal of the colonoscope.

A "complete colonoscopy" was defined as successful insertion to the cecum bottom or terminal ileum. Insertion to the cecum and withdrawal time was recorded for every colonoscopy.

CO_2 insufflation and monitoring system

CO_2 was administered using a commercial CO_2 regulator (Gas Regulator, Crown, Model FR-IIS-P; Yutaka Engineering, Tokyo, Japan) connected to a CO_2 bottle.

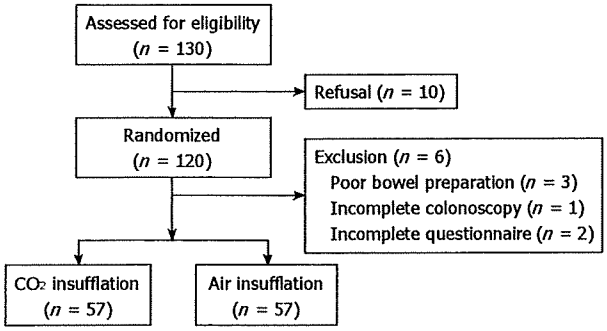

Figure 1 Patient flow chart.

The regulator delivered CO_2 at the rate of 2 L/min. CO_2 and air insufflations were used in a blind fashion both to patients and colonoscopists with full-day colonoscopy sessions randomly assigned CO_2 or air insufflation to avoid unblinding caused by set-up changes between patients.

CO_2 partial pressure was continuously measured using a transcutaneous CO_2 monitoring system (TOSCA 500; Radiometer Basel AG, Switzerland). Processed transcutaneous CO_2 readings ($PtcCO_2$) correlate closely with directly obtained arterial blood gas results[16,17]. Sensors were attached to a patient's ear lobe with a monitor-specific clip. A colonoscopy assistant recorded readings and an independent observer monitored gas readings to avoid potential serious side effects. CO_2 insufflation was stopped immediately if $PtcCO_2$ registered > 60 mmHg during any colonoscopy examination.

Pain and discomfort measurement

A 100-mm visual analogue scale (VAS) consisting of a horizontal line 100 mm in length was used for measuring patient abdominal pain and discomfort (0 mm = painless, 100 mm = extremely painful)[18]. Patients recorded the pain level experienced upon reaching the cecum bottom, immediately following their examinations and 30 min, 1, 2, 4 and 6 h afterwards. The VAS score was the distance measured to the nearest millimeter from the left end of the line to the point of the patient's mark.

Another member of the medical staff, who did not know how the procedures were performed, interviewed the patients 30 min after completion of their colonoscopies. A questionnaire was then given to the patients to take home to complete as instructed at intervals of 1, 2, 4 and 6 h and the completed forms were then mailed to the hospital the following day. The completed questionnaires were subsequently mailed to our medical office. No follow-up phone calls were made as 98% of all questionnaires were promptly returned.

Statistical analysis

A preliminary pilot study was conducted to estimate the SD in pain measurements. With an assumed SD of 19 mm, the study sample size was calculated at 110 patients in order to have an 80% power with two-sided α levels of 0.05 to detect any differences in VAS scores between the two insufflation groups ($\geq$ 10 mm was considered clinically important).

The outcomes for our secondary objective to clarify any differences between the two insufflation methods in relation to the experience level of participating colonoscopists were analyzed on an intention-to-treat basis, given the fact that a number of the initial examining colonoscopists were replaced during the insertion phase of the procedure. Statistical comparisons were made using chi-square and Fisher's exact tests. ANOVA was used for repeated measures statistical analysis of pain. Some variables were not distributed normally, thus the Wilcoxon rank sum test was applied for supplementary analysis to compare groups at each measurement point. Statistical analyses were performed using Prism version 5.0 (GraphPad Software, San Diego, CA, USA) and JMP version 6.3 (SAS Institute, Cary, NC, USA). A P value < 0.05 was considered significant.

RESULTS

Baseline characteristics

A total of 130 patients were asked to participate and 120 consenting patients were randomized into two groups prior to their colonoscopy examinations (Figure 1). Three poor bowel preparation patients were not included and one (0.85%, 1/117) incomplete intubation patient in the air insufflation group with a history of abdominal and pelvic open surgery, whose examination was performed by an EC, was not submitted for consideration. Completed questionnaires were received from 98% of the 116 remaining patients, thus a final total of 114 patients (68% female/32% male) were analyzed in this study. Exactly half or 57 patients were examined using CO_2 insufflation and the other 57 patients were examined with air insufflation. There were no significant differences in baseline patient characteristics including eligibility criteria for potentially difficult cases between the two groups (Table 1).

Outcome measures comparing CO_2 and air insufflation groups

There were no significant differences in procedure times including intubation, withdrawal and total time between the two groups (Table 2). Midazolam was administered to two patients (4%) in each group. There were no instances of $PtcCO_2$ > 60 mmHg in the CO_2 insufflation patients or any procedure-related complications in either group.

Figure 2 shows the mean VAS scores during and after colonoscopy examinations. VAS scores in the CO_2 insufflation group were significantly better than those in the air insufflation group (P < 0.001, ANOVA for repeated measures). The overall mean difference was 5.3 mm (95% CI: 3.5-7.1, P < 0.001). Comparison by nonparametric analysis at each measurement point produced results favoring CO_2 insufflation immediately following the examinations and up to 2 h afterwards. The maximum mean difference of 9.2 mm (95% CI: 0.4-18.0, P = 0.0049) was recorded 30 min after the examinations.

Table 1 Patient characteristics (n = 114) n (%)

	CO_2 group (n = 57)	Air group (n = 57)	P value
Median age, yr (IQR)	65 (59-73)	62 (47-71)	0.107
Females	39 (68)	38 (67)	1.00
Eligibility criteria for difficult cases[1]			
Females with relatively low BMI (< 22)	35 (61)	36 (63)	0.133
Previous abdominal and/or pelvic open surgery	41 (72)	37 (65)	0.546
Males with previously diagnosed left-side diverticulosis	6 (11)	2 (4)	0.271
One or more previous colonoscopies	16 (28)	15 (26)	1.00

[1]Some patients had more than one difficult case factor. IQR: Interquartile range; BMI: Body mass index.

Table 2 Use of antispasmodic drugs at median procedure times for CO_2 or air insufflation groups

	CO_2 group (n = 57)	Air group (n = 57)	P value
Patients receiving antispasmodic drug (%)	54 (95)	56 (98)	0.616
Median total procedure time, min (IQR)	22.5 (17.9-29.6)	22.3 (16.3-43.9)	0.734
Insertion to cecum	10.3 (6.5-16.6)	9.6 (5.8-16.2)	0.601
Withdrawal	11.9 (10.1-13.6)	12.0 (9.8-14.2)	0.986

Table 3 Median procedure times for colonoscopist groups

	EC group (n = 53)	LEC group (n = 61)	P value
Median total procedure time, min (IQR)	19.5 (15.3-25.8)	23.8 (19.2-34.5)	0.005
Insertion to cecum	7.7 (5.1-13.2)	12.5 (7.0-18.9)	0.036
Withdrawal	10.9 (10.0-13.0)	12.5 (10.2-15.1)	0.003
Examiner replaced during intubation	1	5	0.213

EC: Experienced colonoscopist; LEC: Less experienced colonoscopist.

Subgroup analysis

Based on the subgroup analysis relative to experience level of the participating colonoscopists, we evaluated 53 patients (46%) in the EC group and 61 patients (54%) in the LEC group. There were no significant differences in eligibility criteria for potentially difficult cases between the two groups, however, the EC group achieved insertion to the cecum significantly faster, while withdrawal and total procedure times were also significantly shorter than those in the LEC group (Table 3). The number of replacements by another colonoscopist was larger in the LEC group (5) than in the EC group (1), however, there was no significant difference between the two groups.

Figure 3 shows the mean VAS scores for 27 CO_2 insufflation patients and 26 air insufflation patients during and following colonoscopy examinations performed by the EC group. There were no significant differences in the mean VAS scores between the two patient groups

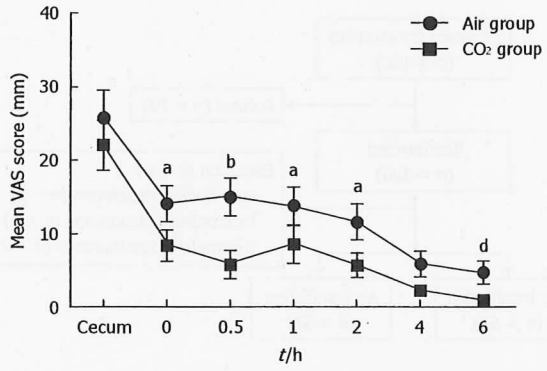

Figure 2 Mean VAS scores at corresponding measurement points during and after colonoscopy examinations in CO_2 and air insufflation groups. VAS scores for CO_2 insufflation were significantly better than those for air insufflation ($^dP < 0.001$, ANOVA for repeated measures). $^aP < 0.05$, $^bP < 0.01$ *vs* the CO_2 group at each measurement point by Wilcoxon rank sum test. VAS: Visual analogue scale.

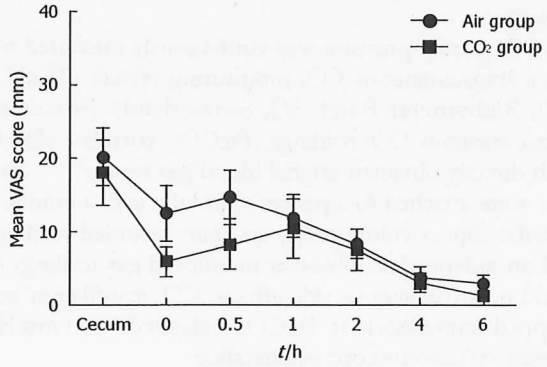

Figure 3 Mean VAS scores at corresponding measurement points during and after colonoscopy examinations for experienced colonoscopists (EC group) in CO_2 and air insufflation groups. There were no significant differences in VAS scores between the two insufflation groups for EC group (P = 0.29, ANOVA for repeated measures).

(P = 0.29, ANOVA for repeated measures). A comparison of the two patient groups at each measurement point also revealed no significant differences. The maximum mean difference of 6.5 mm (95% CI: -3.7-16.6, P = 0.207) occurred 30 min after the examinations.

In the LEC group, 30 CO_2 insufflation patients were evaluated along with 31 air insufflation patients. The mean VAS scores in the CO_2 insufflation group were significantly better than those in the air insufflation group (P = 0.023, ANOVA for repeated measures) (Figure 4). The overall mean difference was 7.5 mm (95% CI: 4.9-10.0, $P < 0.001$). A comparison of the two groups by nonparametric analysis at each measurement point produced results favoring CO_2 insufflation from immediately after the examinations up to 4 h later with the maximum mean difference of 11.6 mm (95% CI: 3.4-19.8, P = 0.006) occurring 30 min after the examinations.

DISCUSSION

The increase in patient abdominal pain and discomfort

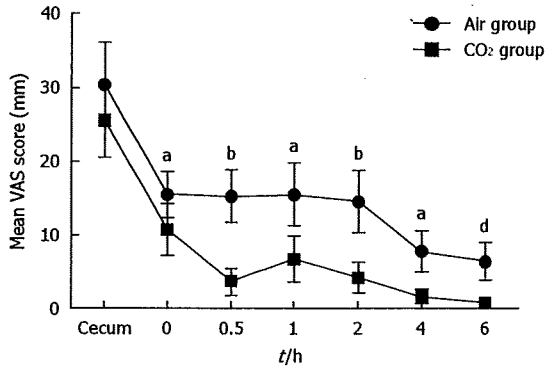

Figure 4 Mean VAS scores at corresponding measurement points during and after colonoscopy examinations for less experienced colonoscopists (LEC group) in CO_2 and air insufflation groups. VAS scores for CO_2 insufflation were significantly better compared to air insufflation for LEC group (^dP = 0.023, ANOVA for repeated measures). $^aP < 0.05$, $^bP < 0.01$ *vs* the CO_2 group at each measurement point by Wilcoxon rank sum test.

often encountered in difficult colonoscopy examination cases is a concern that needs to be satisfactorily resolved by colonoscopists. In this study, we successfully demonstrated the clinical effectiveness of CO_2 insufflation in potentially difficult colonoscopy examination cases. We also clarified the efficacy of CO_2 insufflation for LECs compared to highly ECs.

CO_2 with its characteristic rapid rate of absorption into surrounding tissue has been reported to be more suitable than atmospheric air in various clinical settings[12-15]. In fact, several randomized trials have shown that CO_2 insufflation reduced post-colonoscopy abdominal pain and discomfort compared to conventional air insufflation in ambulatory settings. Bretthauer *et al*[15] demonstrated that CO_2 insufflation was not only effective, but also safe during colonoscopies in patients receiving conscious sedation. Saito *et al*[19] introduced the use of CO_2 insufflation during lengthier colorectal endoscopic submucosal dissections in patients receiving conscious sedation. Their results demonstrated the effectiveness and safety of CO_2 insufflation as well as a resultant reduction in total dosage of midazolam. CO_2 insufflation has also been applied in endoscopic retrograde cholangiopancreatography (ERCP)[20] and endoscopic dilatation therapy using a double balloon endoscope[21]. There have been few detailed investigative reports on the use of CO_2 insufflation during difficult colonoscopy cases. In addition, the effect of the relative experience of colonoscopists using CO_2 insufflation has not been previously analyzed.

This study validated our theory that CO_2 insufflation is more effective than air insufflation in potentially difficult colonoscopy cases with the comparative difference for the two procedures being particularly discernable between LECs and ECs. Colonoscopy is a technically demanding procedure requiring considerable instruction and on-the-job experience for optimal performance. A suitable training program and sufficient opportunities to improve practical skills in a clinical setting are essential for beginners as well as colonoscopists with a moderate degree of experience[10,11,22].

Difficult colonoscopy examinations performed by LECs require additional time as do ERCP and therapeutic endoscopic procedures, and can cause patient abdominal pain and discomfort both during the procedure and afterwards. The results of our study demonstrated a difference not only in intubation times, but also in withdrawal and overall examination times according to the experience of the participating colonoscopists. Avoiding prolonged insufflation especially during insertion, however, might have led to similar results in the LEC group concerning the clinical effectiveness of CO_2 in reducing patient pain and discomfort.

Lee *et al*[8] recommended that trainees perform over 150 examinations in a colonoscopy training program to be technically competent for diagnostic colonoscopy. Our results revealed significant differences in examination times and patient abdominal pain and discomfort after colonoscopy between the EC and LEC groups. The four colonoscopists in the LEC group had each performed a minimum of 900 colonoscopies, thus the question arises as to whether a minimum of 150 cases referred to in the report by Lee above, is sufficient for conducting examinations in potentially difficult colonoscopy cases.

A recent study in Ontario, Canada analyzed factors associated with incomplete colonoscopies based on the following settings: an academic hospital, a community hospital and private medical offices. The incomplete colonoscopy rate was highest in private offices with an odds ratio increase of more than three-fold[3], thus introducing CO_2 insufflation may be particularly useful in reducing patient complaints in non-hospital environments. We refrained from using novice colonoscopists in this study because of the formidable nature of potentially difficult colonoscopy cases. Such novices should only conduct difficult colonoscopies after gaining the necessary experience performing routine colonoscopy examinations.

A number of techniques and devices have reportedly been effective in reducing patient abdominal pain and discomfort during difficult colonoscopies, improving the rate of successful insertion to the cecum, shortening insertion time to the cecum and reducing the dosage of sedatives[23] including the use of a pediatric colonoscope[24], variable stiffness colonoscope[25], gastroscope[26], double balloon endoscope[27] and hood attached to the top of the colonoscope[28]. A PVSC featuring both variable stiffness on demand and a thin diameter was used in our trial. Previously, this instrument was shown not to be superior to adult or standard pediatric colonoscopes[29-32]. However, there have been reports that use of the PVSC made it possible to complete colonoscopies that would have been much more difficult or impossible to perform using an adult colonoscope, including patients who had undergone hysterectomies[31] and patients with diverticular disease and severe stenosis[32].

There was only one case (0.85%) of incomplete insertion to the cecum in our study and just four (3.5%) patients required sedation. Complete screening colonoscopy without sedation or with on-demand sedation in

academic medical centers has been reported to be in the 88%-99% range[33-36], with the optimum intubation rate obtained using a PVSC. In this study, the PVSC more than likely contributed to the impressive successful intubation rates and reduction in pain during insertion to the cecum achieved in both groups, as well as the favorable intubation times for each group. In several studies performed by ECs at academic medical centers, insertion to the cecum times varied between 7-13 min for colonoscopies performed without sedation or with on-demand sedation[33-36]. Our median intubation times of 7.7 and 12.5 min for ECs and LECs, respectively, were in line with these earlier reports.

In conclusion, we clearly demonstrated the clinical effectiveness of CO_2 insufflation in potentially difficult colonoscopy examination cases performed without sedation. We also successfully clarified the efficacy of CO_2 insufflation for LECs.

COMMENTS

Background

Colonoscopy is the preferred method for preventing, detecting and treating colorectal cancer, however, prolonged cecal intubation can cause increased patient abdominal pain and discomfort especially in difficult cases, such as female patients with a relatively low body mass index, patients with a history of abdominal and/or pelvic open surgery and male patients with diverticulosis. CO_2 with its rapid rate of absorption has been reported to be more suitable than atmospheric air as an insufflation agent in various clinical settings, although air insufflation is still the standard method due to a lack of suitable equipment and inadequate information as to when and on whom CO_2 insufflation should be used during colonoscopy examinations.

Research frontiers

This prospective randomized controlled study was conducted to clarify the effectiveness of CO_2 insufflation in potentially difficult cases, particularly in relation to colonoscopist experience level.

Innovations and breakthroughs

The clinical effectiveness of CO_2 insufflation was clearly demonstrated in potentially difficult colonoscopy examination cases performed without sedation. The procedure that was followed also clarified the efficacy of CO_2 insufflation for less experienced colonoscopists (LEC) particularly in comparison to more experienced colonoscopists.

Applications

The use of CO_2 insufflation can be incorporated into existing and future colonoscopy training programs in order to further improve the technical skills of colonoscopists.

Peer review

The authors successfully demonstrated that CO_2 insufflation with its rapid rate of CO_2 absorption and improved efficacy reduced patient pain in potentially difficult cases particularly when colonoscopy examinations were performed by LECs.

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Novel diagnostic methods for early-stage squamous cell carcinoma of the anal canal successfully resected by endoscopic submucosal dissection

Although anal canal squamous cell carcinoma (ACSCC) is quite rare, it can be recognized clearly using iodine staining [1]. Early-stage esophageal squamous cell carcinoma (SCC) has recently been diagnosed using both narrow-band imaging (NBI) [2] and autofluorescence imaging (AFI) [3]. Here we report on the first case of early-stage ACSCC diagnosed by NBI and AFI and treated successfully by endoscopic submucosal dissection (ESD).

A 70-year-old woman was referred to our hospital for treatment of ACSCC. Conventional colonoscopy (PCF-Q240Z, Olympus Optical Co., Tokyo, Japan) revealed a slightly protruded lesion approximately 10 mm in size and located close to the dentate line (**Fig. 1**). The superficial microvessels of the lesion were examined by white light and NBI systems with magnification (**Fig. 2**), and appeared similar to esophageal intraepithelial papillary capillary loops (IPCLs) [4]. The AFI image was purple in color (**Fig. 3 d**), and the lesion was unstained following iodine staining. NBI, AFI, and iodine staining images were similar to those of esophageal SCC (**Fig. 3**) [3,4].

An endoscopic diagnosis of carcinoma in situ was made because of the IPCL-like microvessels; ESD was performed (**Fig. 4**) [5] because the location of the lesion caused technical difficulties in achieving an en-bloc endoscopic mucosal resection. Histopathological analysis of the resected specimen revealed SCC, with microinvasion of 0.4 mm but no lymphovascular invasion (**Fig. 5**). Chemoradiation therapy, with a dose-reduction of 25%, was carried out because of the microinvasion. A follow-up colonoscopy performed 23 months later revealed the ESD scar (**Fig. 6**), and the biopsy specimen was negative for malignancy.

Endoscopic diagnosis of ACSCC and an accurate prediction of invasion were both based on similarity to esophageal IPCLs. En-bloc ESD of early-stage ACSCC followed by chemoradiation therapy resulted in a successful treatment and better patient quality of life; it is possible, therefore, that this could become a standard treatment protocol in the future for early-stage ACSCC.

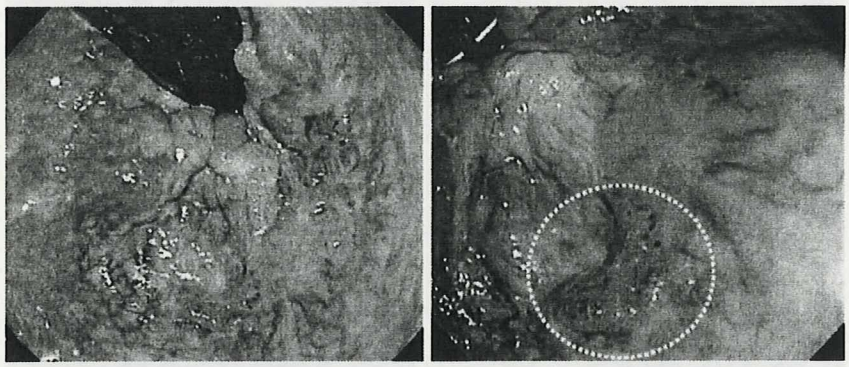

Fig. 1 Conventional colonoscopy showed a slightly protruded lesion (white circle) measuring approximately 10 mm in the lower rectum close to the dentate line.

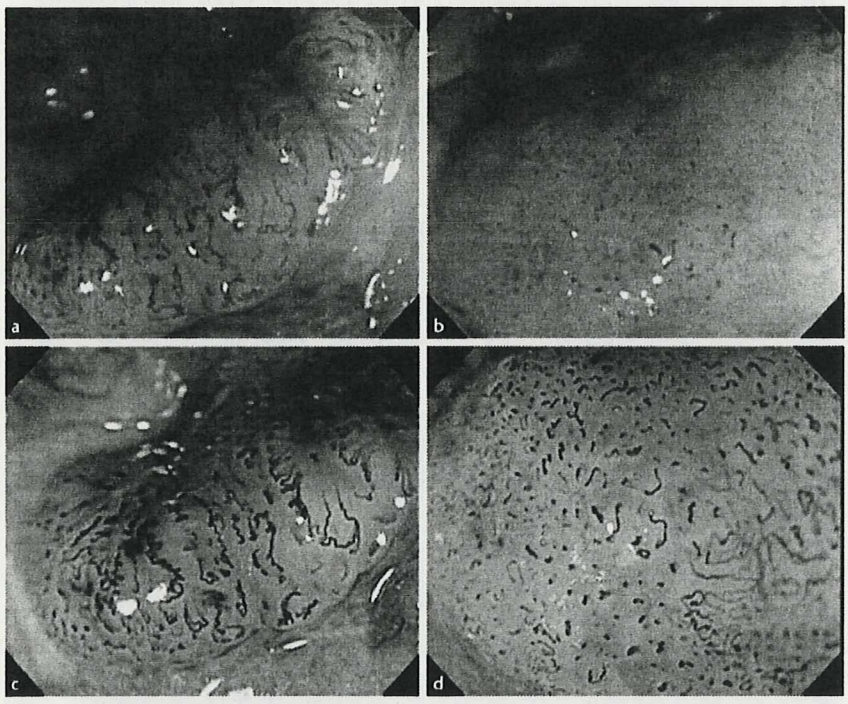

Fig. 2 **a,b** Magnified conventional white light views of the mildly protruded lesion showed dilatation, weaving, and elongation of intraepithelial papillary capillary loops (IPCL)-like microvessels. **c,d** Magnified narrow-band imaging colonoscopic views clearly showed dilatation, weaving, and elongation of IPCL-like microvessels.

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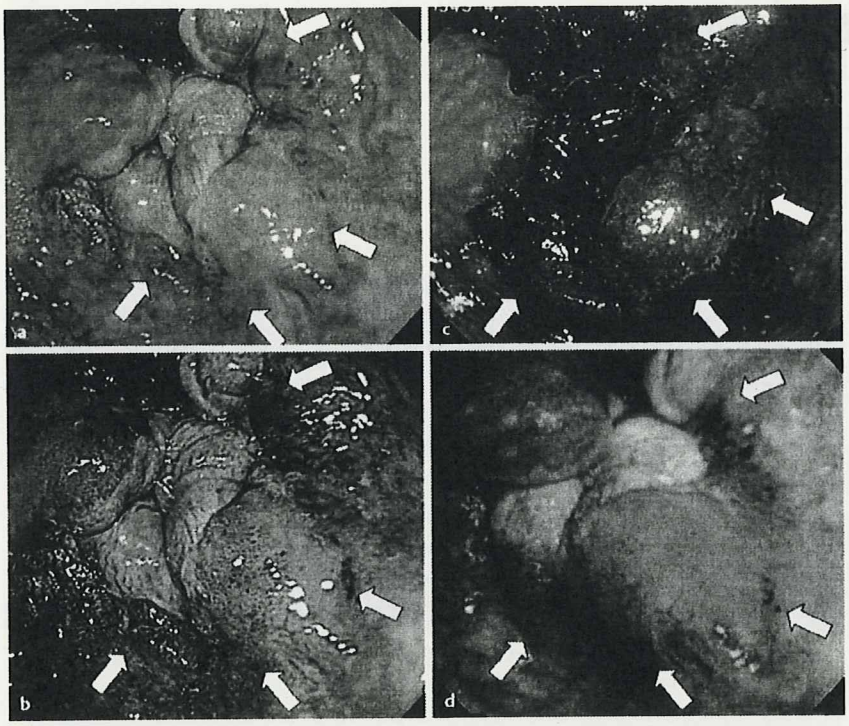

Fig. 3 Different views of the lesion. **a** Conventional white light. **b** Narrow-band imaging. **c** Chromoendoscopy (iodine-staining). **d** Autofluorescence imaging.

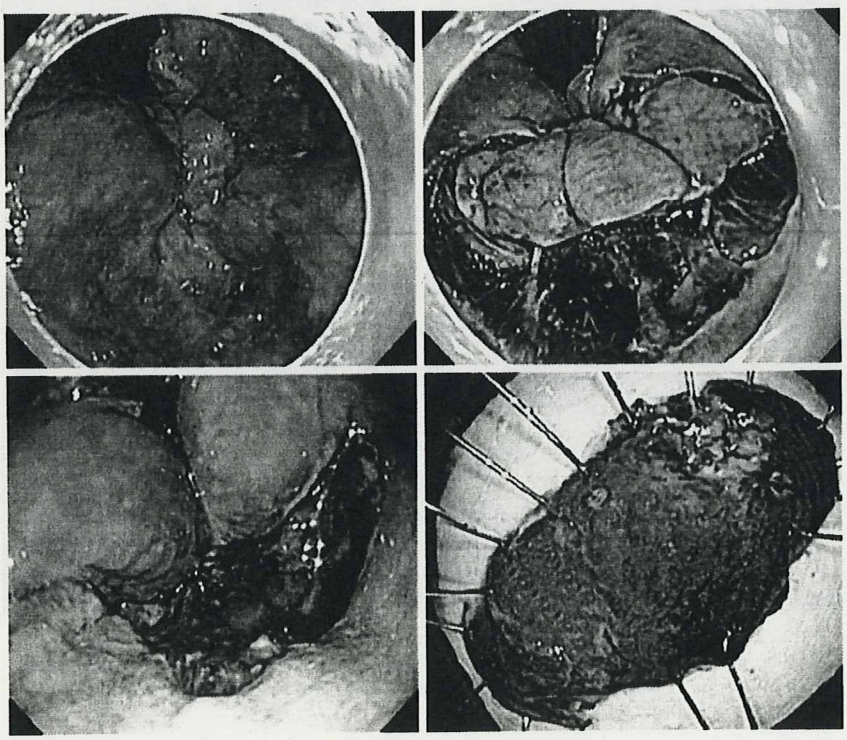

Fig. 4 Pictures of the endoscopic submucosal dissection procedure.

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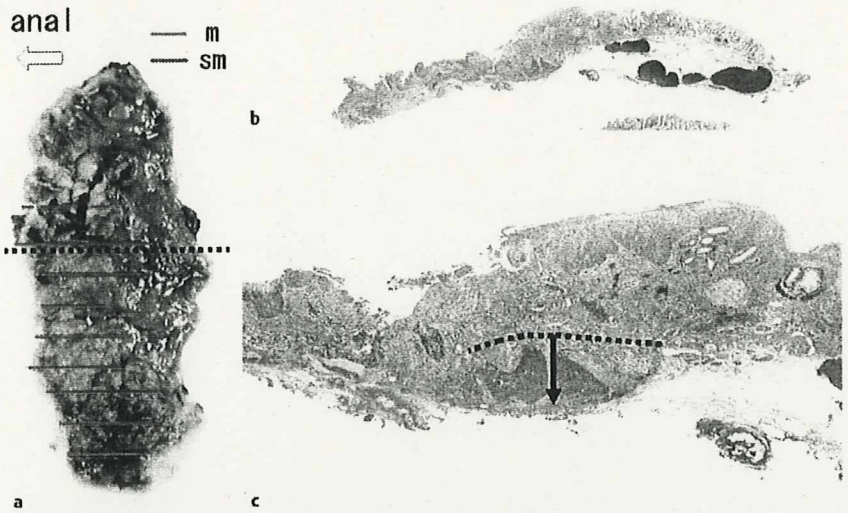

Fig. 5 **a** Resected specimen (10 × 40 mm). Orange lines indicate mucosal (m) cancer areas. The red line indicates the submucosal (sm) invasion area. **b** Hematoxylin and eosin staining. **c** Original magnification of black square shown in **b** (× 80). The submucosal invasion was 0.4 mm, estimated by the putative line extending from the muscularis mucosa of the colorectal mucosa.

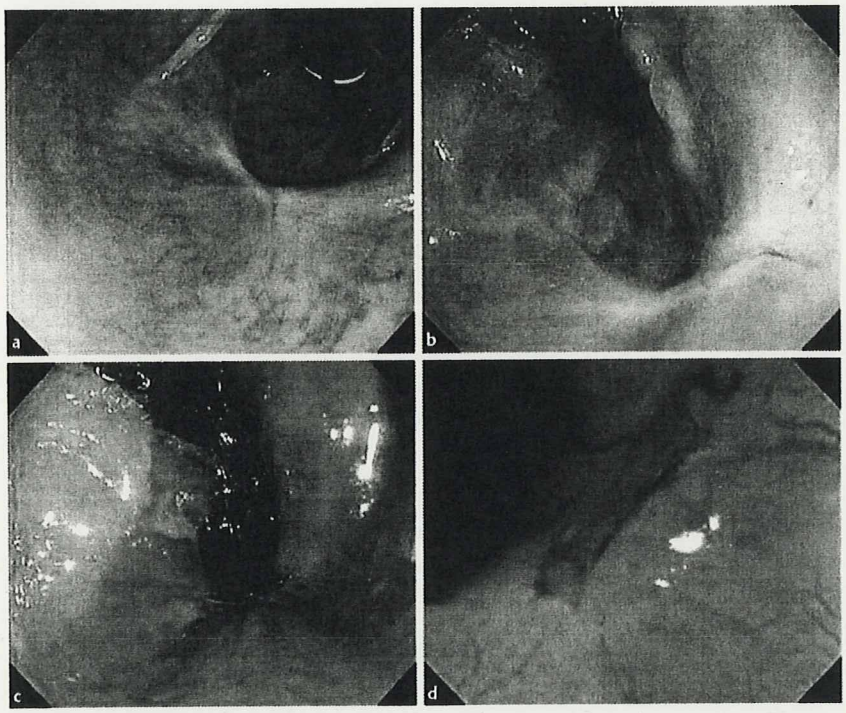

Fig. 6 The follow-up pictures of colonoscopy after endoscopic submucosal dissection and chemoradiation therapy. **a** Conventional colonoscopic view. **b** Close-up conventional colonoscopic view. **c** Iodine-stained chromoendoscopic view. The resection area is shown as iodine-stained. **d** Magnified chromoendoscopic view. The resection was iodine-stained, and there were no abnormal IPCL-like microvessels.

Bibliography
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研究会報告

「さくら消化器内視鏡研究会」について：2005年3月より，年2回，本学消化器肝臓内科，日大医師会，エーザイ (株) の共催にて，毎回テーマを決めて本学板橋，駿河台，練馬光が丘の三病院からの報告，症例検討，ならびに各分野の著名な講師を招いての特別講演を開催している．

大腸内視鏡のA to Z —挿入から診断・治療まで—

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国立がんセンター中央病院内視鏡部

はじめに

大腸内視鏡治療の適応は，大腸腺腫および早期癌の内，リンパ節転移の危険性のほとんど無いと思われる病変である．大腸癌治療ガイドラインでは，粘膜内癌および，SM癌のうち無茎性病変においてはpSM 1000 μm未満の病変 (pSM1) がそれに該当する．粘膜筋板が保持され，脈管浸潤，低分化腺癌を認めないことなどが条件となるが，これらの因子の中で内視鏡的に判断可能なのは深達度のみである．

I. 軸保持短縮法

大腸腫瘍の的確な内視鏡診断および治療を行う大前提として，工藤の軸保持短縮法による挿入が大前提となる．その際，1. スコープは肛門縁から40 cm離してソフトに握る．2. スコープの操作はゆっくり行い，過度なjiggling techniqueは行わない．3. 挿入は自然に腸管内に存在する空気を利用して送気は最小限にする．4. SDを越えるまでは，スコープの回転のみで挿入する．5. スコープの左右アングルと，右手の捻りで左右への回転を行う．と言った点に注意する．RSからSD junctionまでは右旋回を主体としたスコープの回転操作のみで挿入する．しかしながら結腸過長例ではαループ法でS-topをわずかに越えたのちにRight turn shorteningで短縮する．横行結腸においてもスラロームテクニックを駆使して挿入する必要があり，さらに的確な腹壁圧迫，体位変換を頻繁に併用する必要がある．

II. 内視鏡診断

深達度診断に通常内視鏡所見に加え拡大内視鏡所見を重視している．VI-pit patternに領域性を考慮したVi (Invasive) pit pattern (Fig. 1) をSM2以深の指標として臨床的に使用している．

III. 治療方針

2 cm未満の病変，またIpでは2 cm以上においても通常ポリペクトミーあるいは内視鏡的粘膜切除術 (EMR) にて一括切除可能である．一方，表面型病変では2 cmを超えると通常EMRでは分割切除となる場合が多く，中でも側方発育型腫瘍 (Laterally spreadingtumor; LST) では，肉眼型の亜分類によりSM浸潤率・様式も異なってくるため治療方針を考える上で注意すべき病変である (Fig. 2).

IV. 大腸EMR・ESDの適応 (Fig. 2)

LSTについての臨床病理学的検討から，拡大観察にてInvasive patternを認めないことを前提に以下のような治療法選択をとっている．顆粒均一型の場合，腫瘍径に関わらずEMR・EPMRで対応．結節混在型は，粗大結節部を確実に切除する計画的EPMRで対応しているが，30～40 mm以上になるとsm浸潤率が高くなる上，計画的EPMRの困難性からESDの相対適応病変と考えている．LST-NGについては，sm癌の頻度も高くsm微小浸潤部の予測が困難な病変が多いことから，一括切除が望ましい．

V. ESDとEMRの治療成績 (Fig. 3)

対象・方法：20 mm以上の大腸腺腫・早期癌に対して内視鏡治療を行った553病変中，病理学的に大腸癌治療ガイドラインの治癒切除基準を満たし，6ヶ月以上の経過観察が可能であった373病変 (EMR/EPMR: 228病変，ESD: 145病変) を対象とし治療成績を比較した．

結果：EMR/EPMR群，ESD群における一括切除率は33% vs. 84% ($p < 0.001$)．遺残・再発率はそれぞれ14% (観察期間 13.4 ± 7.9) vs. 2% (11.1 ± 7.9)．穿孔 (穿通) は2例 (0.9%) vs. 9例 (6.2%) に，後出血を7例 (3.1%) vs. 2例 (1.4%) に認めた．平均治療時間は108分 vs. 29分であっ

本論文は，第9回さくら消化器内視鏡研究会 (2009年3月5日，日本大学医学部内科学系消化器肝臓内科学分野，日本大学医師会，エーザイ株式会社の共催) での特別講演の要旨である．

(日本大学医学部内科学系消化器肝臓内科学分野　水野滋章，荻原章史，森山光彦)

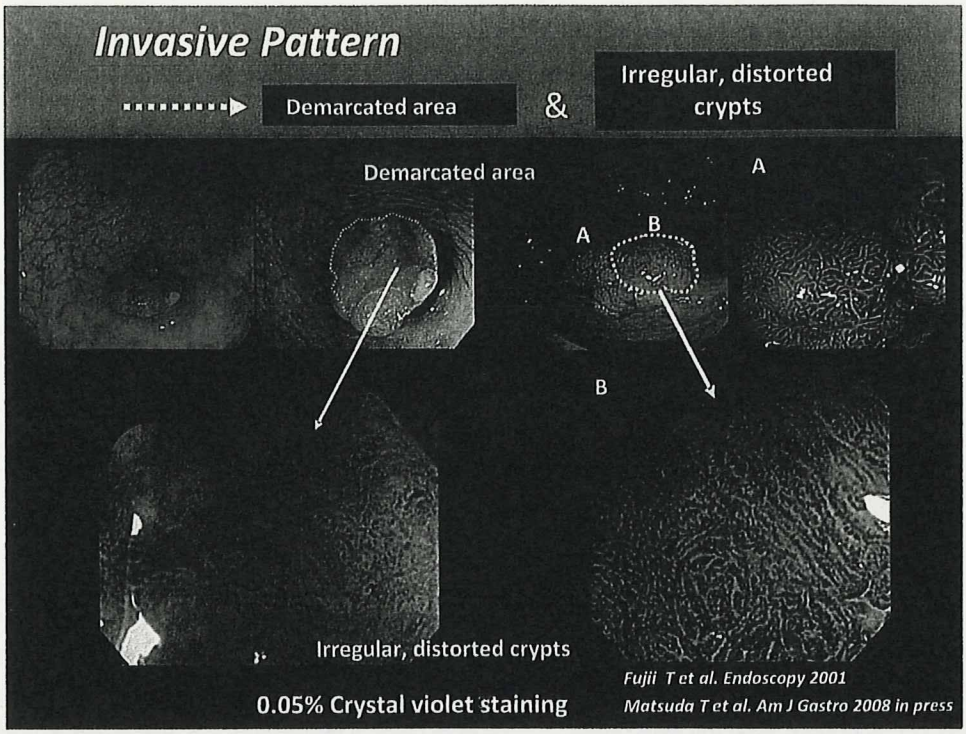


Fig. 1

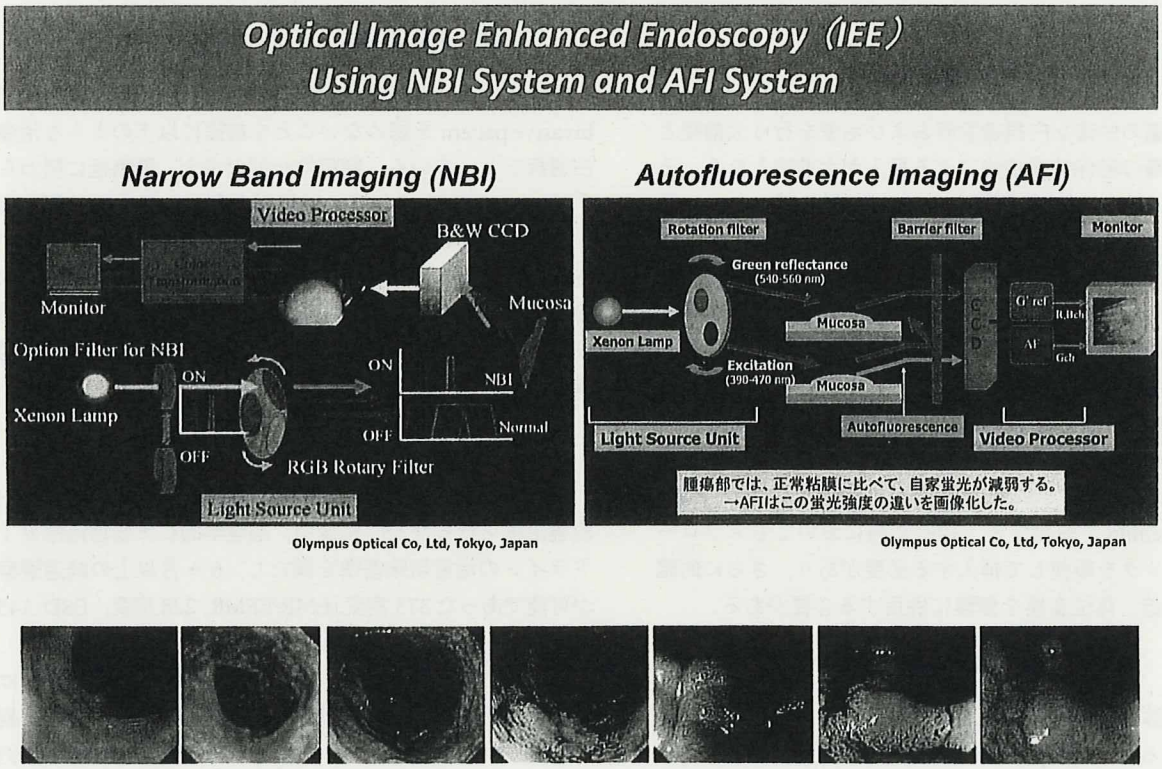
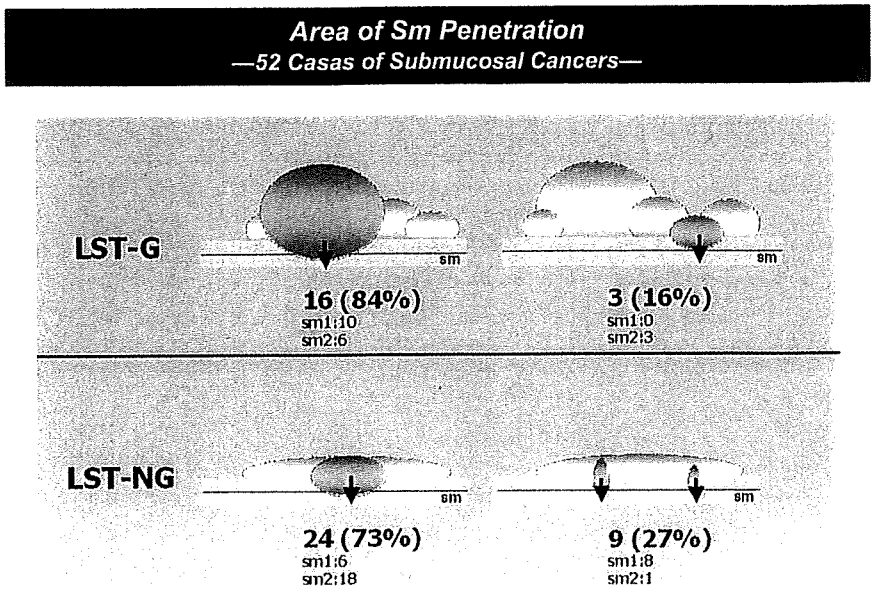


Fig. 4

た ($p < 0.001$)．EMR/EPMR 群の再発例に関しては，内視鏡での追加治療で 94% (31/33) 対処可能であったが，1 例は浸潤癌として再発した．ESD 群ではすべて内視鏡治療で対処可能であった．

VI. 新しい内視鏡技術―光デジタル法 (Fig. 4)

狭帯域内視鏡：Narrow Band Imaging (NBI) や自家蛍光内視鏡：Autofluorescence Imaging (AFI) といった内視鏡が開



Uraoka T, Saito Y, et al. Gut 2006

Fig. 2

EMR と ESD の 治療成績
—20 mm 以上の腺腫・早期癌：経過観察例—

	EMR/EPMR	ESD
Cases	228 (EPMR: 154)	145
Tumor Size (mean ± SD: mm)	28.2 ± 7.9 (20–25)	37.0 ± 14.1 (20–140)
Follow-up Duration (mean ± SD: Month) (median: Month)	13.4 ± 7.9 (6–40) 12	11.1 ± 7.9 (6–44) 6
En-bloc Resection	74 (33%)	122 (84%) $p < 0.001$
Recurrence Rate	33 (14%) EMR: 2 (3%), EPMR: 31 (20%)	3 (2%) $p < 0.001$ En-bloc: 0 (0%), Piecemeal: 3 (13%)
Complications: Perforation Delayed Bleeding	3 (1.3%) 7 (3.1%)	9 (6.2%) $p < 0.001$ 2 (1.4%) *N.S*
Operation Time (mean ± SD: min)	29.0 ± 24.8 (3–120)	108.7 ± 7.1 $p < 0.001$ (15–360)

2003. 1–2006. 12: National Cancer Center Hospital

Fig. 3

発され光デジタル法として注目されている．NBI による腫瘍・非腫瘍の鑑別に関し，佐野らからすでに有用性が報告されている一方，腫瘍の発見率については，欧米から，いくつかの報告があるものの有用性に関して議論がわかれている．浦岡らが行った Back to back による検討では，NBI は通常光と比較し腫瘍径の小さな表面型病変をより多く発見できる可能性が示唆された．AFI に関しても，大腸腫瘍の発見に関する知見が明らかにされつつある．これらの光デジタル法の新しい内視鏡システムを使用することで，今まで発見が困難であった表面型大腸腫瘍の診断が容易になることが期待される．

おわりに

大腸腫瘍に対する内視鏡診断と治療方針について概略を述べた．通常内視鏡診断に加え拡大内視鏡診断などを有効に利用し，腫瘍の臨床病理学的特性を考慮した治療方針を立てることが重要である．

早期大腸癌内視鏡治療の現状と未来

斎藤　豊*
さいとう　ゆたか

- 内視鏡治療の適応はリンパ節転移の危険性がほとんどないと考えられる病変である．現時点では，腺腫・粘膜内癌（M癌）・粘膜下層癌の一部（SM1；粘膜下層浸潤距離1000 μm未満・脈管侵襲（−）・先進部por成分（−））である．これらの因子の中で内視鏡的に術前に診断可能な因子は深達度のみである．
- 深達度診断には通常内視鏡診断・拡大内視鏡診断・超音波内視鏡診断・Non-lifting signなどが用いられているが当院では拡大内視鏡診断を重視している．
- ポリープ型の病変に対してはポリペクトミー・2 cm以下の平坦型病変に対しては内視鏡的粘膜切除術（EMR）が適用されている．2 cm以上の表面型病変に対しては，詳細な内視鏡観察のもと計画的分割切除術（EPMR）が適用されてきた．
- 大腸病変に対しても内視鏡的粘膜下層剝離術（ESD）が可能となり，2 cm以上の側方発育型腫瘍（LST），なかでも非顆粒型LST（LST-NG）に対して適用されている．
- 今後，リンパ節転移の危険因子が病理学的および分子生物学的に解明されることでSM癌の中でもリンパ節転移の危険性がほとんどない病変の抽出が可能となる可能性がある．
- 全層縫合のデバイスが開発されつつあり，大腸においてもESDが標準化し，さらには全層切除術といった新たな治療手技が開発される日も近い．

Key Words　内視鏡的粘膜切除術（EMR），内視鏡的粘膜下層切除術（ESD），内視鏡的計画的分割切除術（EPMR），深達度診断，拡大内視鏡，リンパ節転移

早期大腸癌に対する内視鏡治療は1971年，Deyhle[1]らが高周波電流によるポリペクトミーの方法論を開発したことでその端緒が開かれた．本法の治療学的な意義はMorson[2]らの提唱したポリープ癌化説（polyp-cancer sequence）により支持され，長いあいだ大腸癌における診断・治療の中心的役割を担ってきた．一方，わが国では工藤・藤井ら[3,4]の啓蒙努力により陥凹型早期大腸癌がまれならず存在することが明らかとなり，欧米においてもその臨床的重要性が認識されるようになってきた．この表面型腫瘍に対しては粘膜下に生理食塩水を注入し病変を半球状に隆起させた後にポリペクトミーに準拠して粘膜を切除する内視鏡的粘膜切除術（EMR）が汎用されるようになった[5,6]．20 mm以上の表面型腫瘍に対してもEMRの適応が拡大されるようになったが，通常のEMRでは分割切除（EPMR）となる場合が多く，遺残・再発率が一括切除と比較して高い，また詳細な病理学的検索が困難となる場合があるといった点から，一括切除を目的とした内視鏡的粘膜下層剝離術（ESD）が大腸においても行われるようになった．ESDが早期胃癌や食道癌に対する内視鏡治療としては，ここ数年で急速に普及したことは，保険点数が改定されたことからも明らかである．一方，大腸ESDに関しては，手技の困難性や，穿孔の危険性，また穿孔した場合に腹膜炎を併発する危険性から，一部の施設のみで行われていたが，最近は，胃ESD件数の増加とともに大腸ESDを行う施設も徐々に増えてきているのが現状である．

□ 適応病変（表1）

ESDの適応病変は，腫瘍径以外はEMRの適応病変と同じである．すなわち腺腫を含めた粘膜内病変から，sm1癌（1000 μm未満）までである．2005年7月に『大腸癌治療ガイドライン2005年

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表1　大腸ESDの適応

原則 Non-invasive pattern

絶対適応

- 非顆粒型LST：LST-NG＞20～30 mm
- M～SM1 with Non-lifting sign

相対的適応

- 顆粒型LST：LST-G（Mix）＞30～40 mm
- Large Recurrent Tumor
- Large Villous Tumor

大腸ESDの適応は，臨床病理学的検討から，拡大観察でNon-invasive patternを呈する病変の内，内視鏡的肉眼型と腫瘍径などを考慮して決定される．

度版』が出版され，①脈管侵襲陰性，②癌先進部低分化化陰性であれば，③壁深達度sm1（sm 1000 μm）まではリンパ節転移の危険性が少ないことが示された[7]．これらの組織学的因子の中で治療前に内視鏡で推定可能な因子は壁深達度のみであり当院では拡大内視鏡観察にてVI（invasive pattern）あるいはVN pitを認めないことをEMR/ESDの絶対条件としている[8～10]．

EMRの適応となるいわゆる側方発育型腫瘍（LST）ではその多くが腺腫あるいは腺腫内癌であり，必ずしもすべての病変を一括切除する必要はない．LSTはその表面形態により顆粒型LST（LST-G）と非顆粒型LST（LST-NG）に亜分類され[3,10,11]，*K-ras*，*p53*などの遺伝子の検討からも肉眼形態別に異なる性質を有することが推測されている[12,13]．当院では，内視鏡的，臨床病理的検討から，明らかなinvasive pattern[8～10]を認めない場合に，sm浸潤率が低く，またsm微小浸潤したとしてもその浸潤部位が予測できるLST-Gに対しては粗大結節を分断しないように切除する計画的EPMRで対応可能としている．一方LST-NGにおいては，20 mmを超えた時点でsm浸潤率が20%近くあり，また術前に予測困難なsm微小浸潤を認めることが多くESDなどの一括切除術が望ましいと考える[10,11]．腸管の半周を越えるようなIs＋IIa（LST-G）の治療方針においては意見のわかれるところではあるが，粗大結節を分断しない計画的EPMRも困難であり，浸潤癌として再発した症例も数例報告されているため，当院ではESDの技術が安定した時期よりESDの適応としている[14,15]．他，何らかの線維化によりnon-lifting signを呈する粘膜内病変，内視鏡治療後の遺残・再発病変，villous tumorなどのうち比較的大きな病変にも，ESDが選択される場合がある．

一方，直腸カルチノイドに関してESDを施行している報告もあるが，局所治療の適応が一般的に10 mm以下のびらん・陥凹をともなわない病変であり，そのほとんどが下部直腸に存在することから当院ではEVLデバイスを用いたESMR-L法[16,17]で対応している．一括切除率および断端陰性率もともに100%に近い成績を示し，なおかつ外来で施行可能である．

□ 大腸ESDの最近の進歩

1999年に，直腸表面型腫瘍の内視鏡治療に，われわれはITナイフ®を用いた一括切除の有用性を報告し[18]その後，山本，矢作らが先駆者となり，深部結腸においても局注液やナイフに工夫をし，ESDが積極的に行われるようになった[19,20]．しかしながら，大腸では腸管壁の薄さからくる穿孔の危険性や，管腔が狭いことから内視鏡の操作性が悪いといった技術的困難性から，いまだESDは一般化していない．そこで，大腸ESDを安全に行うため，さまざまな工夫，機器の改良が行われている．

□ 局注液

表面型腫瘍の粘膜下に生理食塩水を注入して病変を隆起させた後にポリペクトミーに準拠して粘膜を切除する内視鏡的粘膜切除術（EMR）が適用されてきたが[5,6]，20 mmを超える病変に対してはEPMRとなることが多い．そこで十分な粘膜下膨隆を長時間維持する目的でグリセオール®の有用性が報告されている[21,22]．しかしながら大腸においてESDを行うにはグリセオール®だけでは十分でなく，さらに粘稠度の高い局注液が必要となり山本[19]らが大腸ESDに使用しているヒアルロン酸（スベニール®，アルツ®）が必須となっている．以前はヒアルロン酸に関して，大腸EMRへの保険適用が認められていなかったが，最近ムコアップ®が市販され保険適用となった．