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INDICATIONS FOR ENDOSCOPIC RESECTION OF COLORECTAL POLYPS AND SURVEILLANCE GUIDELINES

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We report three keynote lecture presentations from the Endoscopic Forum Japan 2009 at Otaru, Hokkaido, on 1–2 August 2009. We will discuss herein: (i) colorectal cancer screening focusing on a comparison between the National Polyp Study and the Japan Polyp Study; (ii) how to deal with small polyps <5 mm in diameter; (iii) the natural history of colorectal tumor development; (iv) the importance of follow up for local recurrence after endoscopic resection for colorectal polyps; and (v) screening for colorectal cancer using two new modalities, narrow-band imaging and autofluorescence imaging. A questionnaire was completed by everyone involved in the conference and the most important results were reported and then discussed by the participants.

Key words: colorectal cancer, surveillance guidelines, National Polyp Study, Japan Polyp Study, autofluorescence imaging, narrow-band imaging.

INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the USA and Japan. The 5-year survival rate for early-stage cancers is greater than 90%, whereas the 5-year survival rate for those diagnosed with advanced cancer is less than 10%.[1,2]

There is indirect evidence that most CRC develop from adenomatous polyps[3] and that it takes on average 10 years for a <1-cm polyp to be transformed into invasive CRC. The importance of the de novo cancer sequence, however, has been proposed and supported by not only Japanese, but also Western endoscopists based on their clinical experience.[4]

Given the findings that adenomatous polyps are precursors to cancer and that polyps and early cancers are usually asymptomatic, there is a strong rationale to support screening asymptomatic individuals for early colorectal cancer detection and prevention.

We report three keynote lecture presentations from the Endoscopic Forum Japan 2009 at Otaru, Hokkaido, on 1–2 August 2009. In this part of the program, we discussed the indications for endoscopic resection of colorectal polyps and surveillance guidelines.

Comparison of National Polyp Study and Japan Polyp Study

The National Polyp Study (NPS)[5] is used as the basis of recommendations for colonoscopic surveillance after polypectomy and it established an interval of 3 years after removal of newly diagnosed adenomas. The NPS was conducted, however, prior to recent epidemiological studies documenting the prevalence of non-polypoid lesions.[4] Thus, it was necessary to conduct a study similar to the NPS using Japanese-style colonoscopy, which consists of better bowel preparation using polyethylene glycol solution taken in the morning on the same day as colonoscopy and other techniques such as chromoendoscopy.

Matsuda *et al.* conducted a multicenter retrospective cohort study[6] to estimate the incidence of advanced neoplasia including the prevalence of non-polypoid lesions after initial colonoscopy using Japanese-style colonoscopy and to compare the differences among various risk groups. Their study group also started a multicenter prospective randomized controlled trial known as the Japan Polyp Study (JPS) in which the study design was similar to the NPS, but the concept was considerably different using Japanese-style chromoendoscopy.

How to deal with polyps <5 mm in diameter & natural history of colorectal polyp development

There is no question that all neoplastic lesions >5 mm in diameter should be resected endoscopically; however, the necessity of resection for small polyps <5 mm is still controversial.[7] The argument for not resecting colorectal polyps <5 mm is based on the hypothesis that such small lesions develop very slowly and need a long period to become invasive cancers.

Such small polyps, however, should be followed up endoscopically after several years. The natural history for the development of these colorectal polyps is still unclear because follow-up cases for such lesions without endoscopic

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resection are rare so far. A few reports are available from retrospective analysis of X-ray examinations.[8]

Until now, the adenoma–carcinoma sequence has been considered to be the main pathway for carcinogenesis, but the importance of the de novo cancer sequence has been proposed recently.

Follow up for local recurrence after endoscopic resection

Colorectal tumors >2 cm and suitable for endoscopic resection are usually superficial type lesions referred to as laterally spreading tumors (LST).[9,10] Such LST are treated with endoscopic mucosal resection (EMR), however, EMR for LST >2 cm occasionally result in piecemeal resection (EPMR).[11] The problem with EPMR is local recurrences and the difficulty of histological evaluation of the piecemeal resected specimens. There have been several reports of local recurrence after piecemeal resections, but the recurrence rate differed among the reports.[11,12] All of the previous reports were retrospective studies so a prospective study is necessary to establish the actual recurrence rate. In addition, endoscopic follow up is necessary within an appropriate period in order to manage local recurrence effectively.

Screening for colorectal cancer using two new modalities

For colorectal cancer screening, colonoscopy is considered the best method demonstrating the highest accuracy, sensitivity and specificity. High-definition colonoscopy[13] has been developed recently enabling colonoscopists to detect even small lesions, however, some flat and depressed lesions are still quite difficult to detect.

The autofluorescence imaging (AFI) (Olympus Medical Systems, Tokyo, Japan)[14] and narrow-band imaging (NBI) (Olympus Medical Systems) video endoscope systems[15–17] have recently been developed as non-invasive optical-digital techniques. It has been reported that both systems have an advantage over standard white light colonoscopy (WLC) and, therefore, may be more effective for the detection of colorectal adenomas.[16]

The AFI video endoscope system is an illumination method that allows for real-time WLC. Neoplastic areas involve a thickening of the mucosal layer and increased hemoglobin, so such areas emit weaker autofluorescence compared to non-neoplastic areas. Recently, the AFI system has been used to enhance detection of early neoplastic lesions in the esophagus, stomach and colon.

The NBI system is another novel optical-digital imaging process that uses special narrow-band filters in the endoscopic system to provide a more detailed visualization of the mucosal architecture and capillary pattern. As a result of the improved mucosal contrast provided by NBI, this technique also has the potential for improving the detection of colorectal lesions compared to standard WLC. NBI still remains somewhat controversial,[18,19] however, because some NBI reports from Japan and the UK have been positive but others from Western countries have been negative for polyp detection.

RESULTS OF QUESTIONNAIRE & DISCUSSION

Only one-third of the Japanese participants in the conference have guidelines for the resection of colorectal polyps <5 mm in diameter. Most participants resect such lesions case-by-case. In summary, it appears that there is no general agreement at the present time and this topic will require further study in the future before a consensus can be reached.

Sixty-three percent of the Japanese participants perform follow-up colonoscopy after 6 months for EPMR cases. In contrast, both of the Asian participants follow them up after 3 months (Fig. 1a). There is no definite evidence as to whether 3 months or 6 months is the better follow-up period. From our retrospective analysis, most recurrences were observed 6 months after EPMR and were treated successfully with repeat endoscopic resection.[12]

Concerning the treatment strategy for residual or recurrent tumors after EPMR, most participants chose endoscopic submucosal dissection (ESD)[20,21] or conventional EMR depending on the recurrent tumor characteristics with only one participant choosing surgery (Fig. 1b). Important factors for the treatment decision are tumor size, histology and tumor location. Appropriate colonoscopic follow up is necessary.

Most Japanese and Asian participants use NBI for targeted digital chromoendoscopy meaning that WLC is used for observation first and only when a polyp is detected, WLC is changed to the NBI mode and a detailed observation of the capillary pattern is performed. Interestingly, only 20% of the participants think that NBI will completely replace the role of indigo-carmine dye spraying (Fig. 1c).

For colorectal polyp detection, 25% of Japanese and 50% of Asian participants regarded NBI as useful in only some cases (Fig. 1d). Most Japanese participants regarded NBI as very useful for the differential diagnosis between non-neoplastic and neoplastic lesions, however, only one of two Asian participants regardeded NBI as being very useful for that purpose probably because NBI is not commonly used outside Japan at this time (Fig. 1e).

As for the possibility of estimating depth of diagnosis using NBI, the participants were undecided. Most participants thought NBI was useful for the depth of diagnosis of early colorectal cancer in some cases, but not for all cases (Fig. 1f). Five out of eight (63%) Japanese participants thought AFI was useful for polyp detection in some cases especially for flat lesions (Fig. 1g). Interestingly, five out of eight Japanese participants also thought AFI was useful for the differential diagnosis between non-neoplastic and neoplastic lesions. Unfortunately, AFI is only available in some Japanese institutions at this time so the data from the Asian participants was used only as a reference.

As for depth diagnosis, most participants thought AFI was not useful. NBI and AFI are considered very useful in some clinical settings, however, both will require further improvements and refinements in the future before widespread use not only in Japan, but also outside Japan.

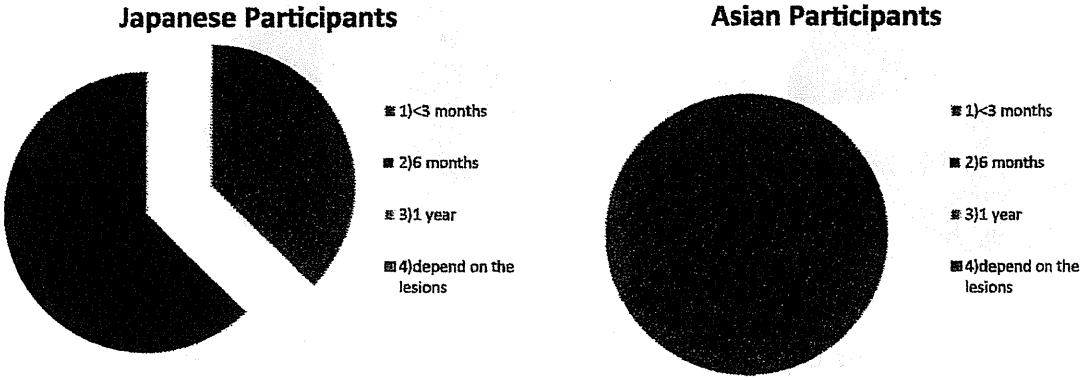
ACKNOWLEDGMENTS

We would like to thank the doctors listed below for their excellent presentations and insightful scientific discussion.

In this preview, all reported information was based on an extensive questionnaire with data collected from the nine

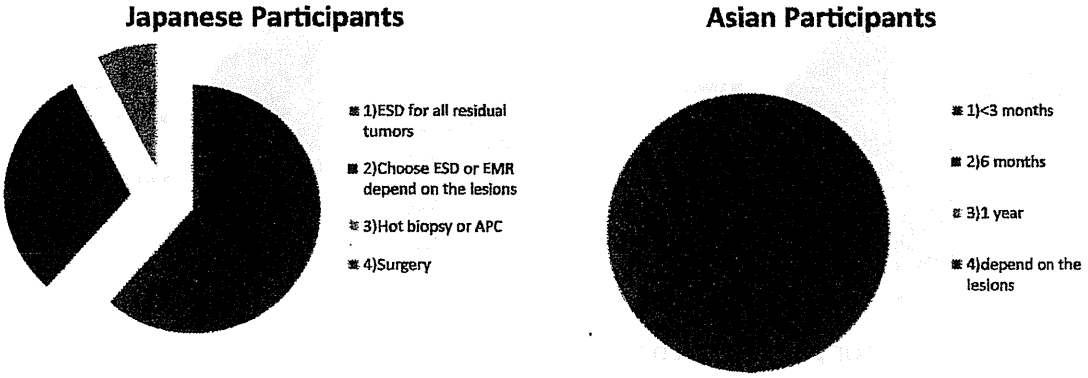
Question 1 a

How many months after piecemeal endoscopic mucosal resection (EPMR) do you perform follow-up colonoscopy ?



Question 1b

How do you treat residual/recurrent tumors after EPMR?



Question 1c

Will NBI replace indigo-carmine dye spraying?

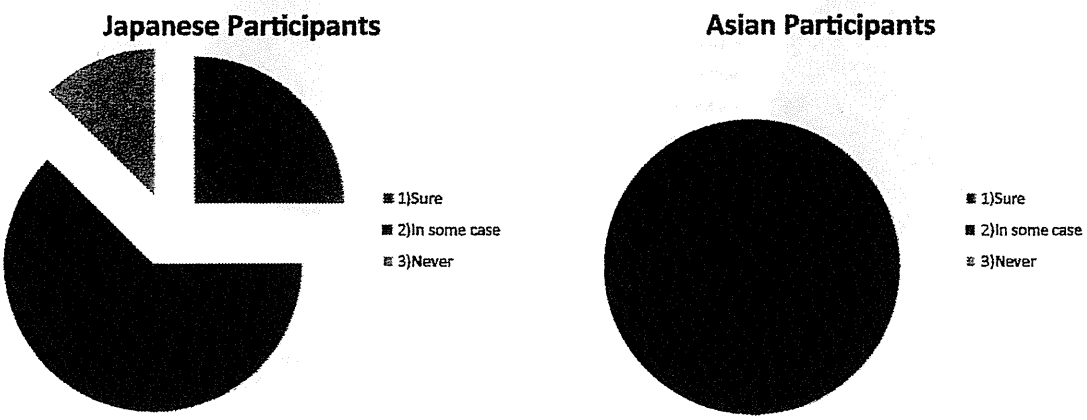
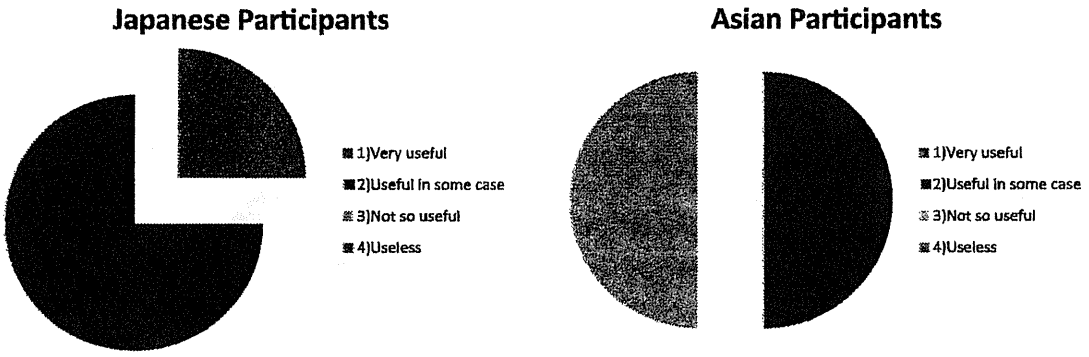


Fig. 1. Results of questionnaire. AFI, autofluorescence imaging; APC, argon plasma coagulation; EMR, endoscopic mucosal resection; EPMR, endoscopic piecemeal mucosal resection; ESD, endoscopic submucosal dissection; NBI, narrow-band imaging.

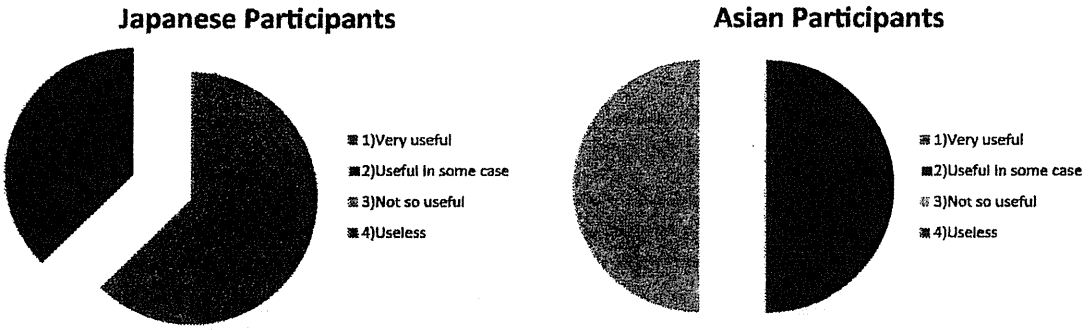
Question 1d

Is NBI useful for polyp detection?



Question 1e

Is NBI useful in the differential diagnosis between non-neoplastic and neoplastic lesions?



Question 1f

Is AFI useful for polyp detection?

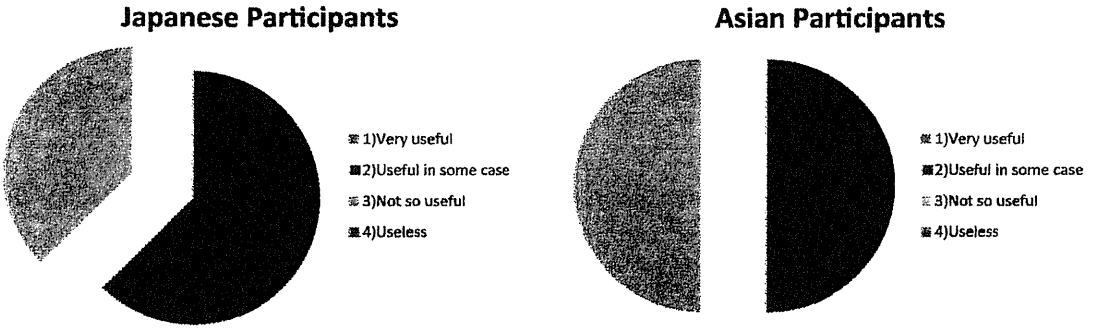


Fig. 1. *Continued*

Japanese participants and the two participants from Singapore and Korea.

Keynote lecturers

Lecture 1 – "How colorectal polyps are treated in Singapore"
Choon Jin Ooi, MD, Singapore General Hospital
Lecture 2 – "How colorectal polyps are treated in Korea"
Dong-Kyung Chang, MD, Samsung Medical Center
Lecture 3 – "Comparison of NPS and JPS"
Takahisa Matsuda, MD, National Cancer Center Hospital

Chairs

Hiro-o Yamano, MD, Gastroenterology Center, Akita Red Cross Hospital
Yutaka Saito, MD, Endoscopy Division, National Cancer Center Hospital

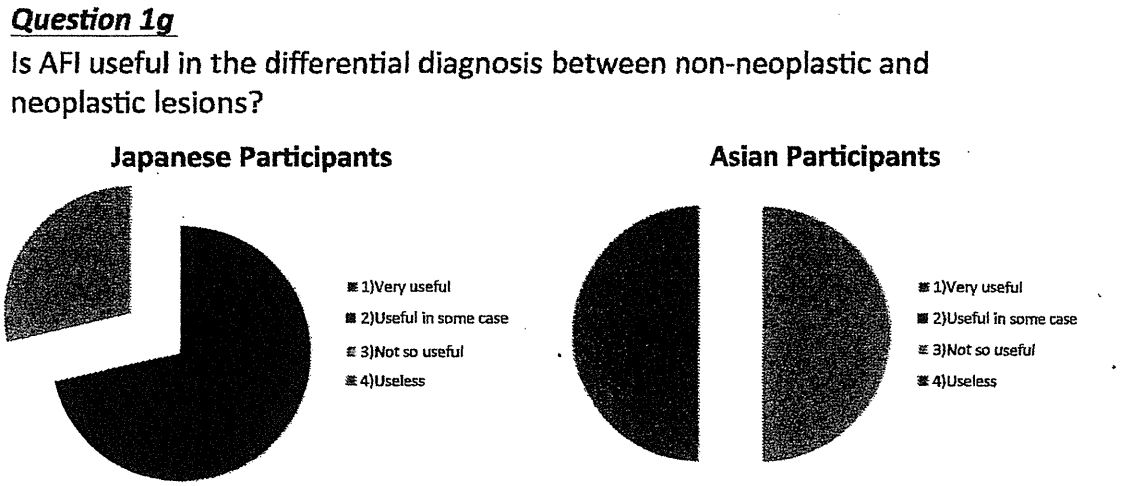


Fig. 1. *Continued*

Additional participants

Toshio Uraoka, MD, Okayama University
Sei Kurokawa, MD, Sapporo-Kosei General Hospital
Youji Takeuchi, MD, Osaka Medical Center for Cancer and Cardiovascular Diseases
Takashi Hisabe, MD, Fukuoka University Chikushi Hospital
Kinichi Hotta, MD, Saku Central Hospital
Takayuki Matsumoto, MD, Kyushu University

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Feasibility of endoscopic mucosal resection for superficial pharyngeal cancer: a minimally invasive treatment

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Background and study aims: New diagnostic techniques have recently been developed so detection of superficial pharyngeal cancer is dramatically increasing and endoscopic mucosal resection (EMR) can now be performed on an experimental basis. The aim of this study was to clarify the effectiveness of EMR for superficial pharyngeal cancer.

Patients and methods: Between 2004 and 2007, 31 patients with 37 pharyngeal lesions underwent EMR at our hospital. EMR using a cap-fitted endoscope (EMR-C) was used on 34 lesions and strip biopsies on the remaining three. We retrospectively assessed the effectiveness of those procedures in treating superficial pharyngeal cancer.

Results: Median procedure time was 45 minutes (range 20–180 minutes) and median hospital stay was 7 days (range 4–12 days). Regarding complications, one patient experienced laryngeal edema, one suffered aspiration pneumonia, and two sustained dermatitis around the mouth caused by Lugol staining. Histologically, 18 lesions were confirmed as carcinoma in situ and the other 19 lesions demonstrated microinvasion of the subepithelial tissue with lymphatic invasion in one case. During the median follow-up period of 40 months (range 21–62 months), two patients received radiotherapy and two patients underwent an additional EMR because of recurrent tumors. Five other patients developed metachronous superficial pharyngeal cancers, but all those lesions were resected primarily by EMR while two of the study's 31 patients died from esophageal cancer. None of the remaining 20 patients experienced any recurrent or metachronous tumors during their follow-up periods.

Conclusions: Our results indicated that EMR was a safe, effective, and minimally invasive treatment for superficial pharyngeal cancer.

Introduction

Although it is possible for gastrointestinal endoscopists to detect pharyngeal cancers, the early detection of superficial pharyngeal cancer by conventional white light endoscopy is extremely difficult because there are so few morphological changes [1,2]. For the detection of esophageal cancers, the widespread use of Lugol staining in high risk populations such as heavy drinkers and heavy smokers is recommended because that technique improves the endoscopic visualization of lesions and often makes it possible to diagnose esophageal cancer at an early stage [3–5].

Unfortunately, there has been no similarly effective diagnostic technique available until quite recently for the detection of pharyngeal cancer at an early stage. Lugol chromoendoscopy cannot be done since it causes severe mucosal irritation leading to significant patient pain and discomfort and can even result in aspiration into the airway [2]. The majority of pharyngeal cancers were previously detected at an advanced stage, therefore, and treated by surgical resection, resulting in both a lower quality of life and a poor prognosis for the patient [6–9]. Two new diagnostic techniques, magnifying endoscopy and narrow band imaging (NBI) [2,10–12], have recently been developed, however, and detection of superficial pharyngeal cancer is now increasing dramatically. Extensive surgical resection for pharyngeal cancer causes loss of swallowing and/or speaking functions and can also lead to cosmetic deformities [6–9]. The development of a new, minimally invasive treatment modality, therefore, was highly desirable for treating pharyngeal cancer. Endoscopic mucosal resection (EMR) is now considered to be one of the possible treatments not only for superficial esophagogastric cancer [13–18], but also for superficial pharyngeal cancer [2,19–22]. Although the feasibility of EMR for superficial esophagogastric cancer has been validated, EMR for

superficial pharyngeal cancer is still an experimental treatment. The aim of this study, therefore, was to determine the short-term outcome of EMR for superficial pharyngeal cancer to help clarify its clinical effectiveness.

Patients and methods

Patients

Between March 2004 and August 2007, EMR was performed by gastrointestinal endoscopists at the National Cancer Center Hospital in Tokyo on 31 men (mean age 64.4 years, range 52–77) with 37 superficial pharyngeal cancers. Of the patients, 30 had either synchronous (n = 14) or prior esophageal carcinomas (n = 16) and only one patient experienced any symptom (throat discomfort) related to pharyngeal cancer. The demographic characteristics of the patients are shown in ○ **Table 1**.

In an effort to clarify the clinical effectiveness of EMR for superficial pharyngeal cancer in this study, we retrospectively assessed the clinical characteristics of the EMR procedures, the histological features of the pharyngeal cancers, and the short-term outcomes. The study protocol was approved by the medical ethics committee of our hospital, and the risks and benefits of EMR were explained to every patient and written informed consent was obtained from each of them beforehand.

Table 1 Clinical characteristics of patients.

Age, years	
Mean	64.4
Range	52–77
Sex	
Men	31
Women	0
Esophageal cancer	
Present	30
Synchronous	14
Prior	16
Absent	1

Definition of superficial pharyngeal cancer

According to the Japan Society for Head and Neck Cancer [23], a superficial pharyngeal lesion is defined as one in which invasion depth is comparatively limited and visual changes do not indicate an advanced cancer. The pharynx has no muscularis mucosae so this somewhat vague definition suggests that depth of invasion is limited to the epithelium or just beneath the epithelium, but does not extend to the muscle layer.

Indications for EMR of pharyngeal cancer

The inclusion criteria for EMR of pharyngeal cancer in our hospital were: (i) endoscopic diagnosis of superficial pharyngeal cancer, and (ii) no findings of lymph node or other organ metastasis at computed tomography (CT).

EMR of pharyngeal lesions was excluded in the case of: (i) a large bilateral hypopharyngeal cancer, or (ii) a hypopharyngeal cancer involving the larynx, because of the possible occurrence of laryngeal edema after EMR of such lesions; (iii) advanced stage pharyngeal cancer; or (iv) pharyngeal cancer with lymph node and/or other organ metastasis regardless of invasion depth. Either radiotherapy (chemoradiotherapy) or surgical resection with lymphadenectomy was indicated for such lesions.

EMR procedures

Lesions were removed using conventional EMR techniques, including EMR using a cap-fitted endoscope (EMR-C) and strip biopsy methods. EMR-C was initially attempted with every lesion, but strip biopsy was subsequently used when injection of saline solution did not sufficiently elevate the mucosa for aspiration into the cap. If any residual tumor was observed on the lateral margin of the ulceration after EMR, electrocautery was also done using hot biopsy forceps.

EMR for pharyngeal lesions was done with the patients either under general anesthesia or intravenous deep sedation using diazepam and pentazocine. With relatively small superficial pharyngeal cancer lesions, when the endoscopist who was to perform the procedures and the consulting head and neck surgeon both judged beforehand that endoscopic treatment could be satisfactorily accomplished in a short time without any complications such as laryngeal edema or aspiration, only intravenous deep sedation was used during the procedures. In the remaining cases where endoscopic treatment was considered to be more difficult, EMR was done with general anesthesia to ensure that the procedures were completed safely. All patients also received local injections of lidocaine mixed with epinephrine-saline solution to anesthetize the mucosa [24].

EMR-C. In this procedure a small specialized plastic cap is attached to the tip of a standard endoscope (Olympus Corp., Melville, New York, USA) (○ **Fig. 1**). After chromoendoscopy using Lugol staining, diluted epinephrine-saline solution with lidocaine was injected into the base of the lesion with a needle. Prelooping, which involved attaching a crescent-shaped snare (SD-221L-25 or SD-7P-1; Olympus Corp., Tokyo, Japan) to the rim of the cap, was done outside the oral cavity. The endoscope was then inserted into the pharynx, the lesion was suctioned into the cap and the snare was pushed down to the base of the aspirated lesion and closed, thereby strangulating the lesion. The suction was released, correct and complete capture of the lesion was assessed and, finally, the lesion was electrosurgically resected [15, 16].

Strip biopsy. This technique requires a double-channel endoscope (2T240; Olympus). After injection, a snare and grasping forceps were each inserted through a channel. The forceps were then passed through the opened snare and the snare was closed lightly around them. An area near the lesion was grasped with the forceps to elevate the lesion, the snare was opened, the lesion was strangulated, and the tumor was then resected by the application of an electrosurgical current [17, 18].

Histological assessment after EMR

Resected specimens were extended on boards with pins and fixed in 10% formalin for 24 hours. After fixation, all resected specimens were cut into 2-mm width longitudinal slices. These were embedded in paraffin and stained with hematoxylin–eosin. Histological assessments that included tumor size, depth of invasion, and vascular invasion were performed microscopically.

Follow-up care

After EMR, each patient underwent both surveillance laryngoscopy and endoscopy at least every 3 and 6 months, respectively. Surveillance endoscopy was done using conventional white light endoscopy until December 2004, but from January 2005, when an NBI video endoscope system was installed in our hospital, most surveillance examinations were done using NBI. A CT scan

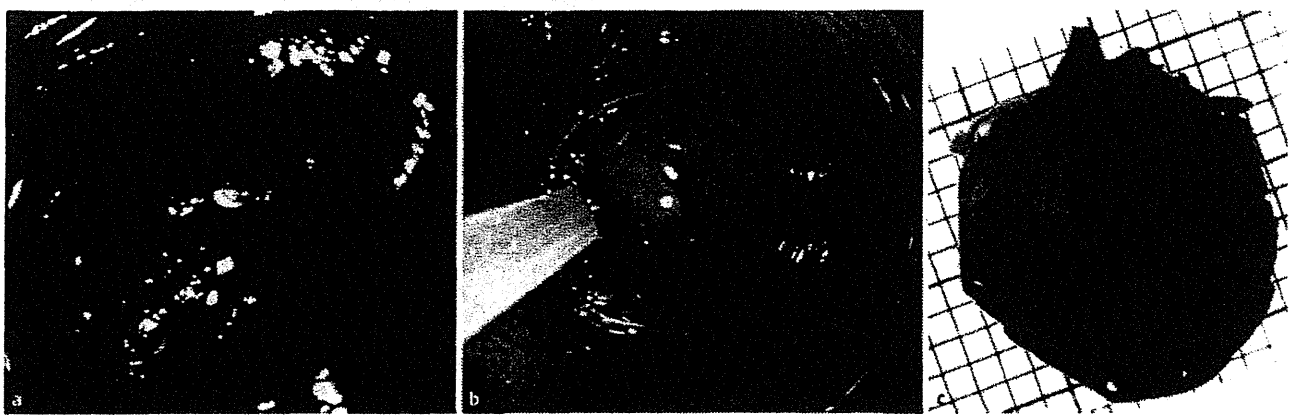

Fig. 1 **a** Superficial pharyngeal carcinoma in right pyriform sinus. **b** Endoscopic mucosal resection with cap-fitted device (EMR-C). **c** Resected specimen.

was also carried out annually to detect any lymph node or other organ metastasis.

A local recurrent tumor was defined as a tumor detected in close proximity to the scar resulting from the EMR, while metachronous tumor was defined as multiple primary tumors detected at other sites away from the location of the EMR scar after more than 6 months.

Results

EMR procedures

EMR-Cs (**Fig. 1**) were performed on 34 lesions and strip biopsies were done for the other three lesions. In addition, electrocautery with hot biopsy forceps was used with four lesions during EMR to treat marginal residual tumor. En bloc resection was successfully done with 16 lesions (43%), while the remaining 21 lesions (57%) involved piecemeal resection with a median number of three pieces per EMR (range 2–11 pieces). Details of the EMR procedures are shown in **Table 2**. The median procedure time was 45 minutes (range 20–180 minutes). With 21 patients (68%) EMR was done with general anesthesia, while 10 patients (32%) had intravenous deep sedation using diazepam and pentazocine.

All 31 patients required hospitalization with a median stay of 7 days (range 4–12 days). Regarding complications, one patient experienced laryngeal edema requiring overnight intubation (**Fig. 2**), another patient suffered from aspiration pneumonia, and two patients sustained dermatitis around the mouth caused by backflow of Lugol stain from the pharynx. None of the remaining 27 patients had any complications other than throat pain and discomfort which were relieved by nonsteroidal anti-inflammatory drugs. The laryngeal edema and aspiration pneumonia were successfully managed using steroids and antibiotics, respectively, while recovery from the dermatitis was achieved without medication. As a result, all 31 patients were discharged without further complications or any loss of function in terms of swallowing or speaking.

Histological results

Histological findings for the superficial pharyngeal cancers are shown in **Table 3**. Of the 37 lesions, 30 (81%) were located in the hypopharynx and seven (19%) in the oropharynx. The pyriform sinus was the most frequent primary site (25, 68%) and the median tumor diameter was 13.5 mm (range 4–40 mm). Histolo-

Table 2 Clinical characteristics of endoscopic mucosal resection (EMR) procedures.

Lesions	
Procedure type, n	
EMR-C	34
Strip biopsy	3
Plus electrocautery with hot biopsy forceps	4
EMR resection type, n	
En bloc resection	16
Piecemeal resection	21
Pieces per EMR piecemeal resection	
Median	3
Range	2–11
Patients	
Procedure time, minutes	
Median	45
Range	20–180
<30	2
≥30 and <60	17
≥60	12
Sedation during EMR, n	
General anesthesia	21
Intravenous deep sedation	10
Hospital stay after EMR, days	
Median	7
Range	4–12
<7	10
≥7 and <10	15
≥10	6
Treatment-related complications	
Present	4
Absent	27

Fig. 2 Complication of laryngeal edema after endoscopic mucosal resection (EMR) required overnight intubation.

Table 3 Lesion characteristics.

	n
Primary site	
Hypopharynx	
Right pyriform sinus	12
Left pyriform sinus	13
Posterior pharyngeal wall	2
Postcricoid area	3
Oropharynx	
Uvula	3
Lateral wall	4
Tumor size, mm	
Median	13.5
Range	4–40
< 10	10
≥ 10 and < 20	14
≥ 20 and < 40	12
≥ 40	1
Histology	
Carcinoma in situ	18
Microinvasion (μm)	19
< 500	9
≥ 500 and < 1000	3
≥ 1000	7
Vascular invasion	
Present	1
Absent	36

gically, all 37 lesions were diagnosed as squamous cell carcinomas (SCCs) with 18 (49%) confirmed as carcinoma in situ and the other 19 (51%) indicating microinvasion of the subepithelial tissue. One of those microinvasive lesions revealed lymphatic invasion, but the remaining 36 lesions had no lymphovascular involvement. Representative endoscopic and histological images of the superficial pharyngeal cancers are shown in **Fig. 3** and **4**.

Follow-up

Follow-up and further treatment outcomes are summarized in **Fig. 5**. Three patients underwent additional radiotherapy either because of recurrent tumors (n = 2) or the presence of lymphatic invasion (n = 1), while two other patients underwent an additional EMR because of recurrent tumors (**Fig. 6**). Five patients developed metachronous superficial pharyngeal cancers, but all those lesions were successfully removed by subsequent EMR (n = 4) or partial surgical resection (n = 1). The two patients who died from esophageal cancer were excluded from the follow-up analysis. Thus, 20/31 patients had no recurrent or metachronous tumors during the median follow-up period of 40 months (range 21–62 months). Likewise, none of the 29 surviving patients had lymph node or other organ metastasis during this median follow-up period.

Discussion

Based on the results of our study, EMR performed by gastrointestinal endoscopists was a safe, effective, and minimally invasive treatment for superficial pharyngeal cancer. Since the median procedure time was only 45 minutes and the median hospitalization period was just 7 days, the physical burden on patients that would have otherwise been associated with their treatment was notably reduced. Although laryngeal edema, aspiration pneumonia, and dermatitis caused by Lugol staining were major complications, all such cases were successfully managed in a short period and every patient was discharged without further complications or the loss of any swallowing or speaking function. In addition, only four of the 31 patients experienced any recurrent tumors during the median follow-up period of 40 months and those patients were treated by either additional EMR (n = 2) or radiotherapy (n = 2). All five cases of subsequent metachronous cancer were detected at an early stage and treated by either local resection with EMR (n = 4) or partial surgical resection (n = 1). These results indicated, therefore, that EMR was both a safe and an effective technique for resection of superficial pharyngeal cancer.

Widespread use of Lugol staining of the esophagus in populations at high risk for esophageal SCC, such as heavy drinkers and heavy smokers, is recommended because it is generally accepted that Lugol chromoendoscopy facilitates the detection of esophageal SCC at an early stage [3–5]. Since a larger number of esophageal cancers can now be detected at an early stage, they are being more widely treated with EMR, resulting in both improved patient prognosis and a better quality of life [15–18].

Early detection of superficial pharyngeal cancers by laryngoscopy or conventional endoscopy is extremely difficult [1,2] so previously most pharyngeal cancers were detected at an advanced stage and treated by surgical resection with a resultant poor prognosis and poorer quality of life for patients [6–9]. Diagnostic techniques such as magnifying endoscopy and NBI [2,10–12] have been developed relatively recently, however, so detection of superficial pharyngeal cancers that can be successfully treated by EMR has been increasing dramatically [2,19–22]. NBI is a novel optical imaging system, using reflected light to visualize superficial tissue structure, that has shown promising results in the diagnosis of both esophageal and pharyngeal cancer. Until recently, we had always sprayed Lugol solution just before performing EMR, but we now believe that NBI will replace Lugol chromoendoscopy as the most effective and noninvasive diagnostic technique for esophageal and pharyngeal cancers, as the availability and use of NBI for diagnosis of these and other cancers becomes more widespread. In such circumstances, the development of a new, minimally invasive modality for the treatment of pharyngeal cancer is also highly desirable. It has previously been reported that superficial pharyngeal cancers have been successfully treated using only EMR, but few reports actually described those procedures in detail [2,19–22]. This study indicating that EMR was a safe, effective, and minimally invasive technique for such cancers, is therefore particularly significant.

Several authors have reported that SCC of the esophagus was often associated with synchronous or metachronous malignancy of other organs including gastric cancer, head and neck cancers and, especially, pharyngeal cancer [25–28], a phenomenon referred to as field cancerization. In this study, 30 of 31 patients had either synchronous or prior esophageal cancers so our results suggest that in order to make an early diagnosis of pharyngeal cancer, endoscopic examination of the pharyngeal mucosa is important, not only for patients with synchronous esophageal cancer, but also for patients previously treated for esophageal cancer.

In addition, we performed follow-up surveillance laryngoscopy and endoscopy at least every 3 and 6 months, respectively, after EMR. Such regular periodic examinations resulted in the early detection of recurrent or metachronous lesions so that those lesions could also be treated primarily by EMR. There are no reports at the present time, however, that establish an appropriate follow-up period after EMR for diagnosing recurrent or meta-

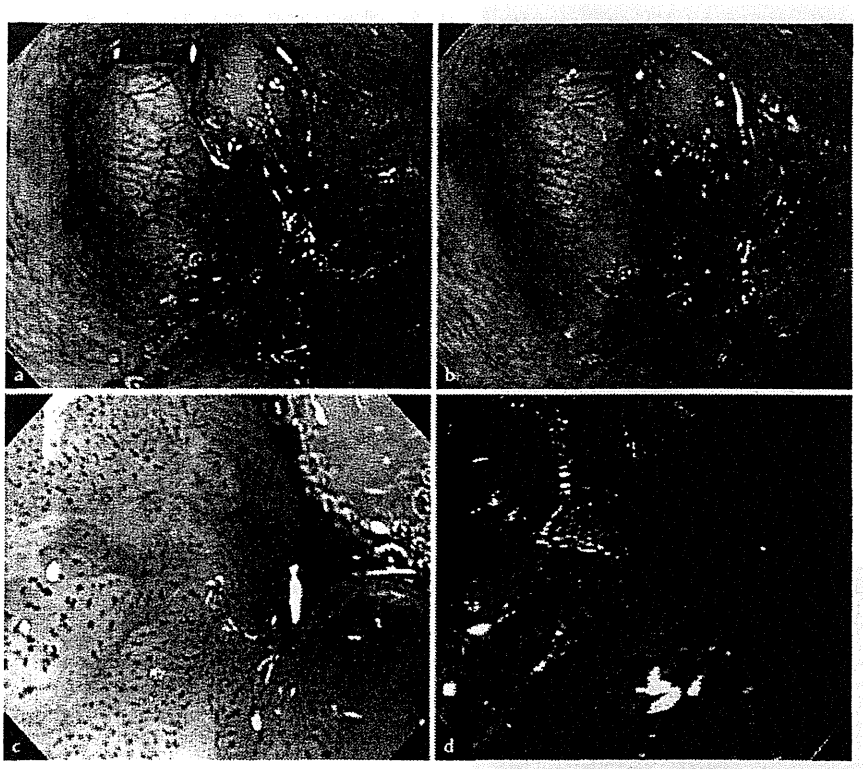

Fig. 3 **a** Conventional endoscopy showed a slightly reddish area in the right pyriform sinus. **b** Narrow band imaging (NBI) endoscopy revealed a clearly demarcated area brownish in color. **c** NBI with magnifying endoscopy highlighted the characteristic changes of intraepithelial papillary capillary loops (IPCLs), including dilatation, tortuosity, and caliber change in a single IPCL, and variation in the shape of multiple IPCLs. **d** Lugol chromoendoscopy with the patient under intubation delineated the lesion margin more clearly.

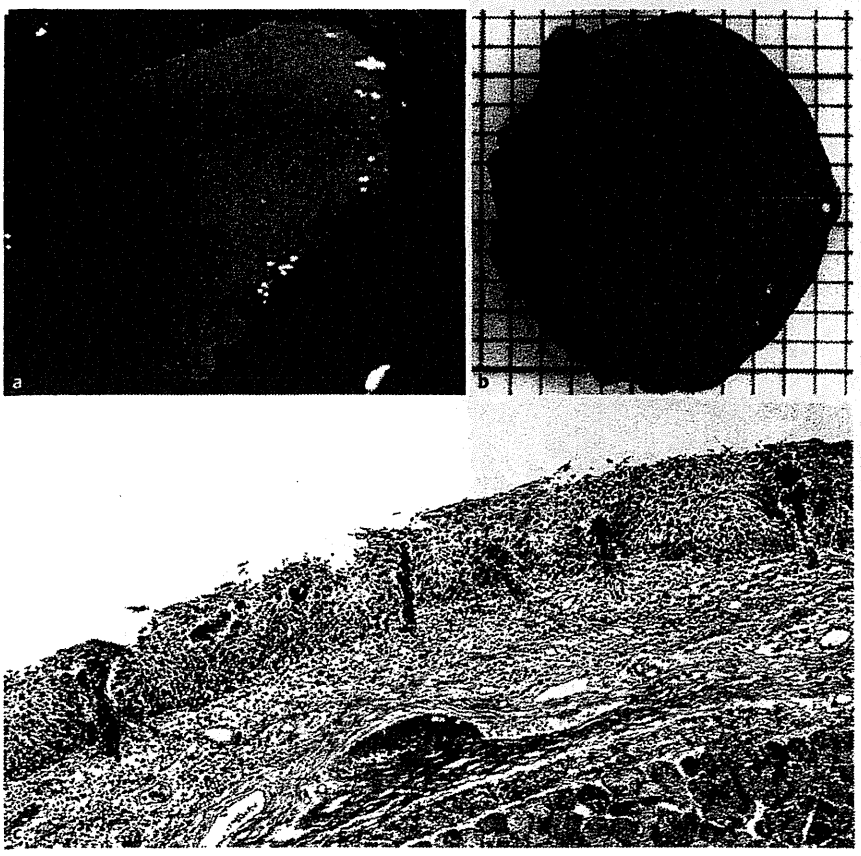

Fig. 4 **a** Another superficial pharyngeal carcinoma in the right pyriform sinus. **b** The resected specimen. **c** Resected specimen revealed squamous cell carcinoma in situ with characteristic intraepithelial papillary capillary loop (IPCL) changes.

chronous lesions at an early stage, so further investigation is needed in this area.

Although using one of the new diagnostic modalities such as NBI enabled us to detect small superficial pharyngeal cancers less than 5 mm in diameter, it has not been determined whether we should treat such lesions immediately, because no reports have been published as yet on how long it takes for superficial pharyngeal cancer to progress to an advanced cancerous stage. It may not be necessary to treat such lesions immediately, but further elucidation as to the nature of pharyngeal cancer is needed to

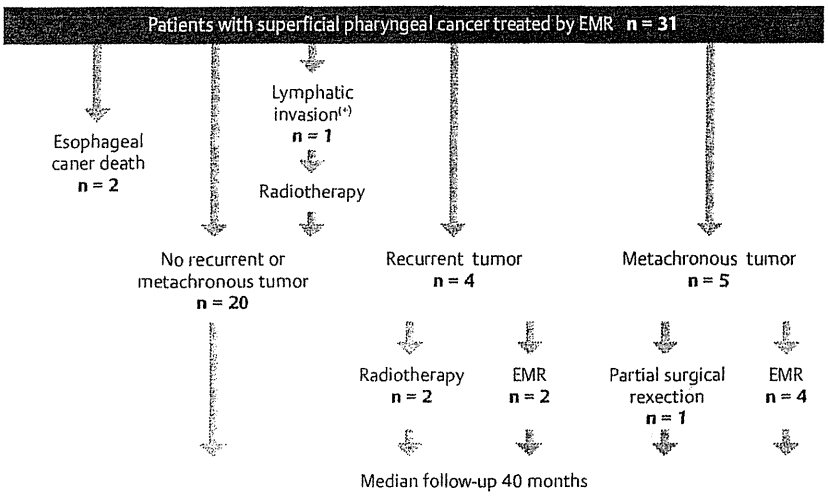

Fig. 5 Follow-up results and further treatments. EMR, endoscopic mucosal resection.

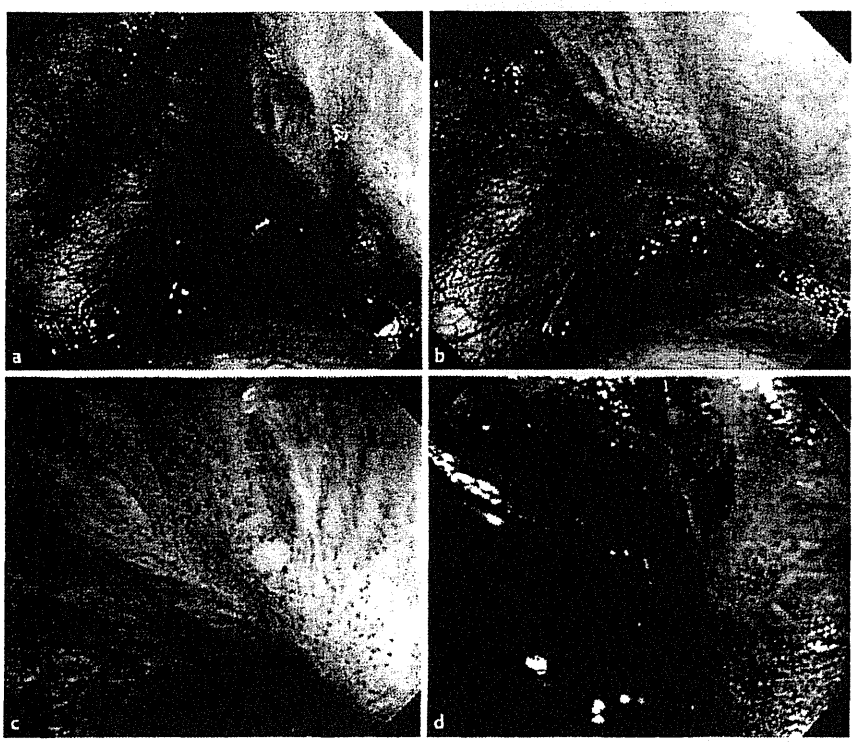

Fig. 6 Local recurrence of pharyngeal carcinoma after endoscopic mucosal resection (EMR) detected near to the EMR scar: **a** conventional endoscopy view; **b** narrow band imaging (NBI) endoscopy appearance; **c** NBI with magnification endoscopy; **d** Lugol chromoendoscopy appearance.

help clarify both the appropriate form and the timing of treatment.

It seems reasonable to conclude from this study that EMR is a safe, effective, and minimally invasive treatment for superficial pharyngeal cancer, but long-term outcome data, including information concerning recurrent and metachronous tumors as well as lymph node and other organ metastasis, are still lacking. While both carcinoma in situ and slight carcinoma invasion of subepithelial tissue seem to be appropriate indications for EMR, there is little reported evidence supporting these criteria [2, 19–22]. A long-term follow-up study to establish the indications for EMR of pharyngeal cancer, therefore, should be conducted in the future to properly evaluate the suitability of EMR for treating superficial pharyngeal cancer.

Endoscopic submucosal dissection (ESD) also has recently been reported to be effective in the en bloc resection of superficial pharyngeal cancers because endoscopists can confirm an accurate cutting line while performing this procedure [20, 22]. It is difficult to maneuver an endoscope and then perform ESD in the oral cavity which is a narrowly restricted and complex area, however, so such lesions are generally resected in several pieces using EMR at the present time. Although piecemeal resections can result in unsatisfactory histological evaluations and increase the risk of local recurrence, all four of the recurrent tumors in our study were detected at an early stage and could be treated by either additional EMR or radiotherapy. Further investigation should also be conducted, therefore, to evaluate the effectiveness of EMR compared with ESD for the treatment of pharyngeal cancers and to determine the most appropriate treatment for such cancers.

The complications encountered in this study were successfully managed within a short period, but EMR for superficial pharyn-

geal cancer must be performed carefully because of the associated risk of laryngeal edema or aspiration into the airway leading to severe respiratory disorders such as pneumonia and suffocation. With every pharyngeal cancer patient who underwent EMR under intravenous deep sedation without intubation, just before EMR we cautiously dripped a small amount of diluted Lugol solution directly onto the pharyngeal lesion itself, using an endoscopic catheter to avoid aspiration into the airway. When EMR was done with the patient was under general anesthesia with intubation, 3% Lugol solution was sprayed on the pharyngeal lesion utilizing the same procedure used during esophageal cancer examinations. We also sprayed thiosulfate solution and saline on the mucosal site after EMR to rinse away the Lugol stain and prevent laryngeal edema. In order to prevent laryngeal edema and aspiration immediately following EMR, we usually provided steroid treatment (intravenous drip infusion and/or inhalant) and administered antibiotics (intravenous drip infusion) for at least 2 days as well. As a further precaution, we normally covered the patient's face, particularly around the mouth, with adhesive tape to prevent dermatitis caused by any backflow of Lugol stain from the pharynx. In order to avoid complications, properly resolve those that do occur, and otherwise minimize the physical burden on patients, it is recommended that endoscopists routinely collaborate with head and neck surgeons when treating such patients in the future.

Finally, it was difficult to maneuver the endoscope in the oral cavity which is a narrowly restricted and complex area. The current EMR procedures need to be refined and/or new techniques developed that provide improved maneuverability before this treatment modality can become accepted for general clinical use. In conclusion, the results of this study indicated that EMR performed by gastrointestinal endoscopists was a safe, effective, and minimally invasive treatment for superficial pharyngeal cancer, but long-term outcome data are still lacking at the present time.

Acknowledgment

▼

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Competing interests: None

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INDICATIONS FOR ENDOSCOPIC RESECTION OF COLORECTAL POLYPS AND SURVEILLANCE GUIDELINES

PREVALENCE AND CLINICOPATHOLOGICAL FEATURES OF NONPOLYPOID COLORECTAL NEOPLASMS: SHOULD WE PAY MORE ATTENTION TO IDENTIFYING FLAT AND DEPRESSED LESIONS?

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Flat and depressed (nonpolypoid) colorectal lesions have been described for over two decades by Japanese investigators. These neoplastic lesions are typically smaller than polypoid ones and can be more difficult to identify during screening colonoscopy. In particular, depressed type colorectal lesions are usually small in size, with a number of studies showing them to be at greater risk for developing high-grade dysplasia or submucosal invasive cancer. It has also been suggested that they may follow a different carcinogenic pathway to flat elevated or protruding adenomas. This paper summarizes recent data of nonpolypoid colorectal neoplasms from Western and Asian countries.

Key words: Japan Polyp Study, nonpolypoid colorectal neoplasm, screening colonoscopy.

INTRODUCTION

Colorectal neoplasms have traditionally been classified in Western countries as sessile or pedunculated. However, in 1983 the Japanese Research Society for Cancer of the Colon and Rectum also recognized the existence of flat adenomas.[1] In 1985 Muto *et al.* described small 'flat adenomas' as lesions <10 mm in size, flat-elevated, sometimes showing a central redness, and with a significant rate of high-grade dysplasia.[2] In regard to depressed lesions, the first reports of depressed (IIc) type colorectal neoplasms were published in 1977 by Kariya *et al.*[3] Following this, IIc type cancers were thought to be a unique 'Japanese phenomenon' until 1993 when Kudo *et al.*[4] reported their depressed type cancer series and classification. Several studies suggested that flat and depressed lesions may behave differently to sessile or protruding lesions, leading more frequently to high-grade dysplasia or submucosal invasive cancer. Since then, many studies have focused on the clinicopathological characteristics of flat and depressed lesions, so-called 'nonpolypoid' colorectal neoplasms.

In 1998, Fujii and Rembacken *et al.* demonstrated depressed lesions in an English population.[5] In this study, 68 adenomas were identified in 47 of 208 patients undergoing colonoscopy: 40% of these adenomas were nonpolypoid. In 2001, Saitoh *et al.* reported the prevalence of nonpolypoid colorectal lesions in North America while Tsuda *et al.* also reported these lesions in Sweden.[6,7] Although initial reports from the Western world suggested a lower frequency of nonpolypoid lesions than in the Japanese series[8] the implementation of chromoendoscopy performed by specialists trained by Japanese experts has improved the detection of such lesions in Western countries.

For screening colonoscopy to become more effective in reducing the incidence and mortality of colorectal cancer, it is important for endoscopists to recognize both polypoid and nonpolypoid colorectal cancer precursors. Left undetected, nonpolypoid colorectal neoplasms may evolve into invasive cancer within a few years following an assumedly normal colonoscopy.[9] This report is intended to provide an overview of the current understanding of the prevalence and clinicopathological features of nonpolypoid colorectal neoplasms.

PREVALENCE AND CLINICOPATHOLOGICAL FEATURES OF NONPOLYPOID COLORECTAL NEOPLASMS

Recent data from Western and Asian countries

In 2000, Rembacken *et al.* reported data from the UK (Table 1).[10] In this prospective study, 1000 consecutive patients attending routine colonoscopy were examined for flat or depressed lesions. Three hundred and twenty-one adenomas and six Dukes' A adenocarcinomas were identified: 204 (62.4%) were polypoid and 37.6% (123) were nonpolypoid lesions. Among all nonpolypoid lesions, the incidence of cancer was 3.3%. However, it was markedly higher in the depressed lesions (50%; 2/4). The authors concluded that the polyp-carcinoma hypothesis prompts colonoscopists to search only for polypoid lesions when screening for cancer, and many early colorectal neoplasms may therefore be missed. Adding to this data are results from

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Table 1. Prevalence of non-polypoid colorectal neoplasms (data from Western and Asian countries)

	No. neoplastic lesions and incidence of Ca (M/SM)					
	All polypoid lesions		All nonpolypoid lesions (0-IIa, IIb, IIc)		Depressed lesions (all IIc)	
	No. lesions (%)	No. lesions with Ca (%)	No. lesions (%)	No. lesions with Ca (%)	No. lesions (%)	No. lesions with Ca (%)
Rembacken *et al.*, UK [10] (n = 327/1000 pts)	204 (62.4)	2 (1.0)	123 (37.6)	4 (3.3)	4 (1.2)	2 (50.0)
Parra *et al.*, Spain [11] (n = 490/1300 pts)	376 (76.7)	10 (2.7)	114 (23.3)	8 (7.0)	3 (0.6)	2 (66.6)
Soetikno *et al.*, USA [13] (n = 1535/1819 pts)	1308 (85.2)	13 (1.0)	227 (14.8)	15 (6.6)	18 (1.2)	6 (33.3)
Chiu *et al.*, Taiwan [14] (n = 5682/12 731 pts)	4653 (81.9)	79 (1.7)	1029 (18.1)	60 (5.8)	39 (0.7)	20 (51.3)

Ca, cancer; M, mucosal invasive cancers; SM, submucosal invasive cancers.

a 2006 Spanish study by Parra *et al.* who reported a review of 1300 consecutive colonoscopic examinations.[11] A total of 490 polyps were adenomas and 150 were hyperplastic; 114 (23.3%) adenomas were flat (three were flat-depressed) whereas 376 (76.7%) were protruding. The diameter of flat and protruding adenomas was 9.2 ± 7.9 mm and 7.0 ± 5.9 mm, respectively ($P < 0.001$). This paper concluded that flat adenomas represent nearly one-quarter of all colorectal neoplastic polyps, their most frequent location being the right colon, and that they bear a higher risk of malignancy than protruding adenomas, especially for the flat-depressed type. From the USA, one study analyzed and reclassified 933 surgically removed sessile adenomas described in the National Polyp Study (NPS) and found no difference between polypoid and flat adenomas with respect to high-grade dysplasia or invasive cancer.[12] However, Soetikno *et al.* recently reported the prevalence and clinicopathological features of nonpolypoid colorectal neoplasms.[13] This was a cross-sectional study at a Veteran's Hospital in California with 1819 patients undergoing elective colonoscopy. Among all neoplasms (n = 1535) detected, 14.8% were classified as nonpolypoid lesions (n = 227, flat: 209, depressed: 18). Overall, nonpolypoid colorectal neoplasms were more likely to contain malignant cells (odds ratio, 9.78; 95% confidence interval, 3.93–24.4) than polypoid lesions, irrespective of the size. The depressed type had the highest risk (33.3%) of cancer. Moreover, Chiu *et al.* recently reported on the prevalence and characteristics of nonpolypoid colorectal neoplasms from Taiwan.[14] This study included 12 731 asymptomatic Chinese subjects (8372 of whom were average-risk subjects) who underwent screening colonoscopy. Nonpolypoid colorectal neoplasm was detected in 4.3% of asymptomatic and 4.2% of average-risk subjects. The prevalence of depressed lesions was 0.18% in both asymptomatic and average-risk subjects. This paper concluded that these findings may lead to modification of screening and prevention strategies for colorectal cancer. Meanwhile, Goto and Oda *et al.*[15] estimated that depressed (IIc), so-called de novo cancer might comprise up to 22.9% of early colorectal cancers (18.6% in men and 27.4% in women) in a cohort of 14 817 Japanese subjects.

Data from National Cancer Center Hospital, Tokyo

Subjects and methods

Between January 1998 and April 2003, a total of 6638 colorectal neoplasms in 3952 patients (men: 2800, women: 1152, mean age [standard deviation]: 63.4 years [9.9]) were treated endoscopically or surgically at the National Cancer Center Hospital, Tokyo. To clarify the importance of nonpolypoid colorectal neoplasms, we classified all lesions into three groups (group A: polypoid [Ip, Isp, Is]; group B: flat [IIa, laterally spreading tumor]; group C: depressed [IIc, IIa+IIc]) based on macroscopic identification during colonoscopy (Fig. 1). In addition, to clarify the clinical importance of flat lesions we further divided these lesions into three groups based on lesion size (Fig. 2).

Results

There were 4471 (67.4%) and 2167 (32.6%) polypoid and nonpolypoid colorectal neoplasms, respectively (Table 2). Among all nonpolypoid lesions, there were 178 (2.7%) depressed lesions, of which 109 (61.2%) were diagnosed as high-grade dysplasia (intramucosal cancer) or submucosal invasive cancer. On the other hand, the incidence of intramucosal cancer or submucosal invasive cancer was 15.4% and 18.9% in polypoid and nonpolypoid lesions, respectively.

Histopathological assessment of all lesions identified 5538 (83.4%) lesions as adenoma (low-grade dysplasia), 851 (12.8%) intramucosal cancer (high-grade dysplasia), and 249 (3.8%) submucosal invasive cancers (Table 3). The prevalence of cancers in our data was extremely high (16.6%) compared to other reports. We considered that this imbalance was related to the specific characteristics of our cancer center being a national referring hospital.

Among the lesions diagnosed as adenoma or intramucosal cancer, the prevalence of depressed lesions was 1.2–1.5%. In contrast, depressed type submucosal cancers were identified in 38.6% (96/249) of subjects. The prevalence of depressed lesions was relatively low compared to polypoid or flat

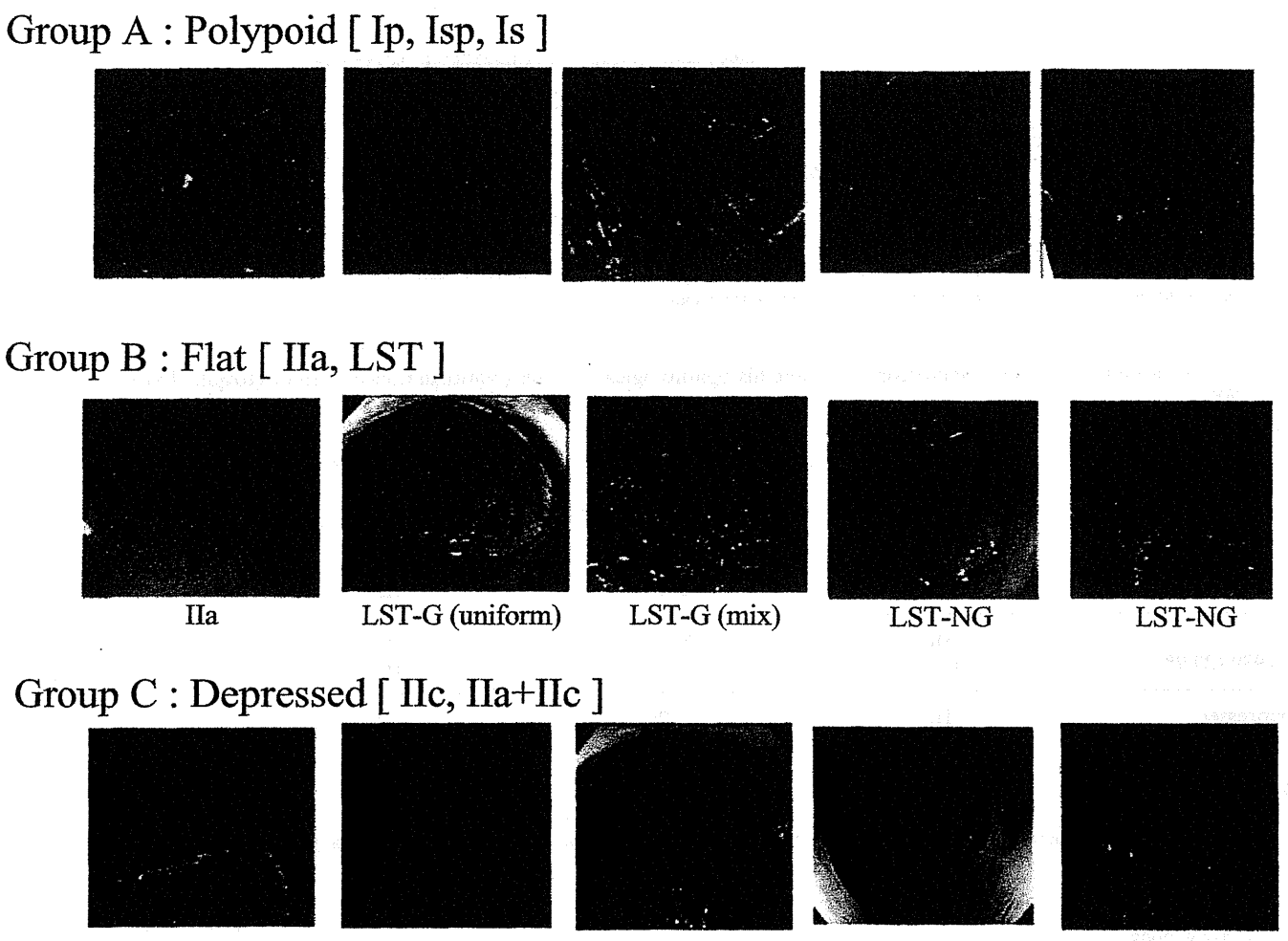

Fig. 1. Prevalence and malignant potential of flat and depressed lesions. LST, laterally spreading tumor (a flat elevated lesion ≥10 mm); LST-G, LST granular; LST-NG, LST non-granular.

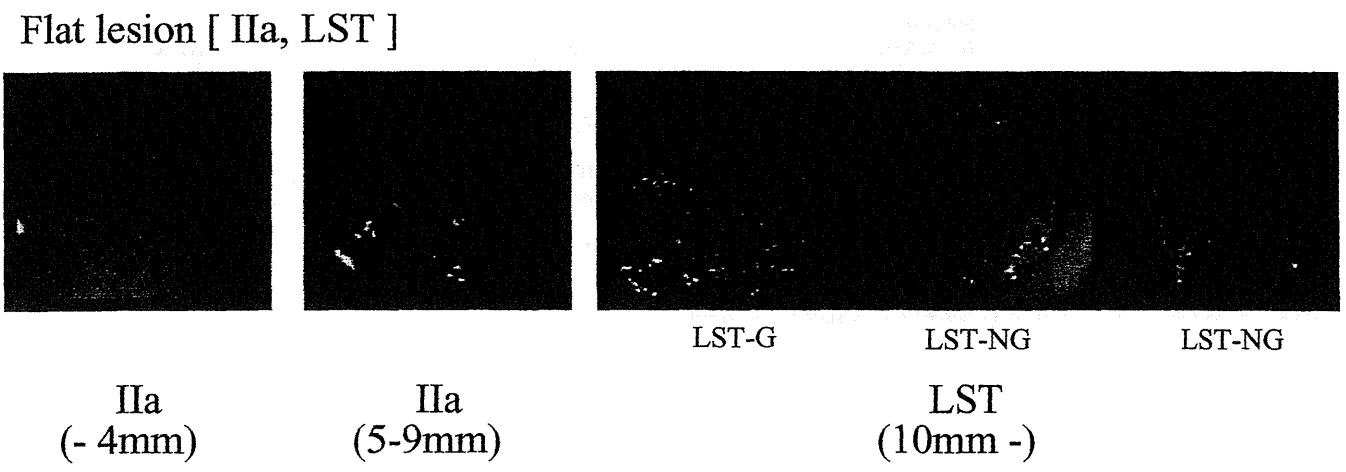

Fig. 2. Flat lesion (IIa, laterally spreading tumor [LST]). LST-G, LST granular; LST-NG, LST non-granular.

Table 2. Prevalence of non-polypoid colorectal neoplasms (National Cancer Center Hospital [NCCH], Tokyo, 1998–2003)

	No. neoplastic lesions and incidence of Ca (M/SM)					
	All polypoid lesions		All nonpolypoid lesions (0-IIa, IIb, IIc)		Depressed lesions (all IIc)	
	No. lesions (%)	No. lesions with Ca (%)	No. lesions (%)	No. lesions with Ca (%)	No. lesions (%)	No. lesions with Ca (%)
NCCH (n = 6638/3952 pts)	4471 (67.4)	690 (15.4)	2167 (32.6)	410 (18.9)	178 (2.7)	109 (61.2)

Ca, cancer; M, mucosal invasive cancers; SM, submucosal invasive cancers.

Table 3. Relationship between macroscopic type and histopathological findings (National Cancer Center Hospital [NCCH], Tokyo, 1998–2003)

	Macroscopic type	Adenoma (LGD)	Intramucosal cancer (HGD)	Submucosal invasive cancer
Polypoid	Ip	360	224	25
4471 (67.4%)	Isp	1053	232	40
	Is	2368	122	47
Flat	IIa	1550	96	11
1989 (29.9%)	LST	138	164	30
Depressed	IIc	26	5	13
178 (2.7%)	IIa + IIc	43	8	83
Total: 6638 lesions		5538 (83.4%)	851 (12.8%)	249 (3.8%)

HGD, high-grade dysplasia; LGD, low-grade dysplasia; LST, laterally spreading tumor, (granular and non-granular).

Table 4. Relationship between lesion size and clinicopathological findings (1989 flat lesions, National Cancer Center Hospital, Tokyo, 1998–2003)

Size	Location (C/A/T: D/S: R)*	Adenoma (LGD)	M-SM Ca (HGD-submucosal invasive cancer)
- 4 mm (830)	508:288:34 (61%:35%:4%)	828 (99.8%)	2 (0.2%)
5–9 mm (706)	387:276:43 (55%:39%:6%)	657 (93.1%)	49 (6.9%)
10 mm - (453)	260:111:82 (57%:25%:18%)	203 (44.8%)	250 (55.2%)
Total: 1989 lesions	1155:675:159 (58%:34%:8%)	1688 (84.9%)	301 (15.1%)

C, cecum; A, ascending; T, transverse; D, descending; S, sigmoid; R, rectum.

lesions (2.7% *vs* 67.4%, 32.6%), however, the incidence of cancer among depressed lesions was significantly higher than that of the other groups.

Regarding flat lesions, there were 830 small (<5 mm), 706 intermediate (5–9 mm) and 453 large (≥10 mm; laterally spreading tumor) lesions (Table 4). As for tumor location, there were 1155 lesions (58%) in the proximal colon, 675 (34%) in the distal colon and 159 (8%) rectal lesions. Among the lesions diagnosed as small, intermediate and large flat lesions, the incidence of cancers (intramucosal cancer or submucosal invasive cancer) was 0.2% (2/830), 6.9% (49/706) and 55.2% (250/453), respectively. Therefore, laterally spreading tumor lesions are undoubtedly clinically more important than small ones.

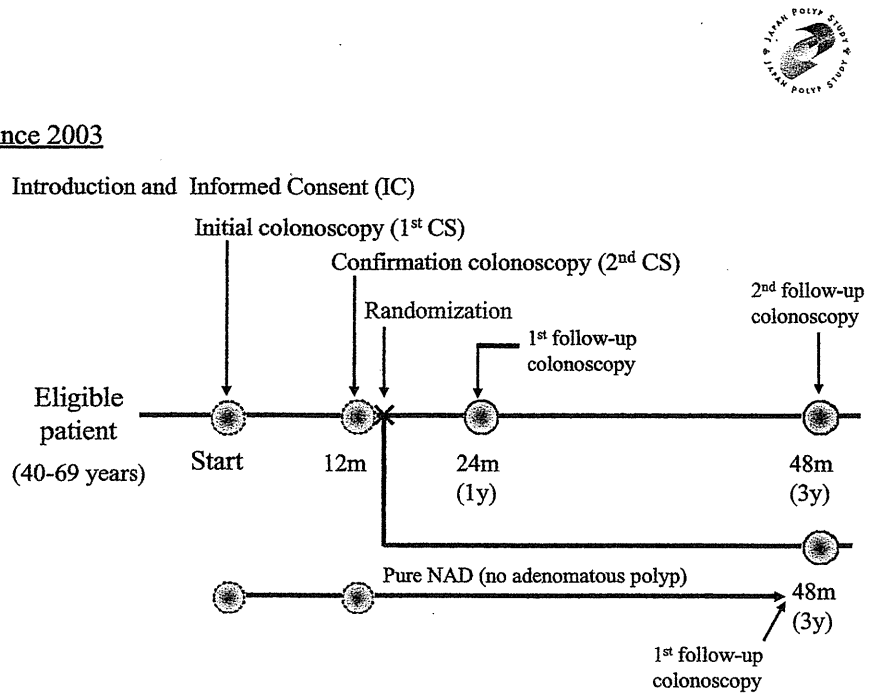

Fig. 3. Schematic overview of the Japan Polyp Study.

CONCLUSION

Although the nonpolypoid (especially depressed type) colorectal neoplasms may be regarded as occurring infrequently, they belong to a distinct subset that demonstrates greater biological aggressiveness, given the high prevalence of intramucosal or submucosal cancers. The detection and diagnosis of the nonpolypoid colorectal neoplasm presents both a challenge and an opportunity. Gastroenterologists need to meet the challenge and become proficient in the endoscopic recognition of these lesions in order to reduce the incidence and mortality from colorectal cancer. Consequently, large-scale prospective data need to be collected to further define the epidemiology and biology of nonpolypoid colorectal neoplasms in all populations. The Japan Polyp Study is a multicenter randomized controlled trial that was initiated in 2003 (Fig. 3).[16] It is prospectively evaluating follow-up surveillance strategies for Japanese populations after complete removal of all polyps, and nonpolypoid colorectal neoplasms, detected by high-resolution chromoendoscopy. The Japan Polyp Study is intended to continue until 2011, and the final step of the randomization process and complete histopathological assessment are ongoing. The clinical significance of nonpolypoid lesions (especially depressed type lesions) in Japan will become clear in this prospective study.

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INDICATIONS FOR ENDOSCOPIC RESECTION OF COLORECTAL POLYPS AND SURVEILLANCE GUIDELINES

LOCAL RECURRENCE AND SURVEILLANCE AFTER ENDOSCOPIC RESECTION OF LARGE COLORECTAL TUMORS

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Local recurrence rates after endoscopic piecemeal mucosal resection (EPMR) typically range from 10 to 23%. In our previous study, the local recurrence rate after a piecemeal resection was significantly higher than that after an en bloc resection, irrespective of tumor size or macroscopic features. To reduce local recurrence after an EPMR, it is important to carefully note the circumferences of the edge and base of the ulcer. Recently, endoscopic submucosal dissection (ESD) was developed and recognized for its effectiveness in large, complete, en bloc resections and precise pathological assessments. ESD also showed lower local recurrence rates, ranging from 0 to 3% in previous, retrospective studies. However, ESD showed a higher perforation rate and longer procedure times; thus, it is necessary to improve ESD. An appropriate surveillance interval after EPMR was still controversial, and recommendations of some guidelines ranged from 2 to 9 months. In order to determine the appropriate interval, a randomized controlled study is necessary.

Key words: colorectal tumor, endoscopic mucosal resection, endoscopic submucosal dissection, local recurrence, surveillance.

INTRODUCTION

Both the incidence and mortality of colorectal tumors have increased recently; currently, colorectal cancers are the first and fourth leading causes of cancer mortality in Japanese women and men, respectively.[1] Large colorectal tumors are typically defined as ≥20 mm in diameter.[2–4] Some large colorectal tumors are adenomas or non-invasive cancers that can be treated successfully with endoscopic resection. Laterally spreading tumor (LST) were described as extending laterally, rather than vertically, and tended to remain in the mucosa.[5,6] Several issues need to be considered in the treatment of large colorectal tumors, including the indication for endoscopic resection, selection of an endoscopic treatment method, the risk of local recurrence, and the surveillance interval. Here, we present a review of the literature and discuss these issues.

INDICATION OF ENDOSCOPIC RESECTIONS

Endoscopic resection is indicated for early colorectal tumors that show negligible risk of lymph node metastases. The conditions for lymph node metastases were studied in a Japanese multicenter survey of colorectal cancers.[7] Based on the report, the pathological conditions that indicated no or low risk of lymph node metastasis included a shallow invasion depth (<1000 μm), no lymphatic invasion, and no sprouting.[7] Of these factors, only the invasion depth can be estimated before treatment. A biopsy is undesirable because it may complicate an endoscopic resection.[8] Furthermore, it is difficult to precisely diagnose the depth of invasion based on a biopsy. In general, a conventional, white light, endoscopic evaluation is used to assess early colorectal cancers; findings of hardness, fold convergence, depression, and irregular shape are considered indicative of submucosal invasion.[9] In pedunculated lesions, a thick stalk and jagged shape are important indications of stalk invasions. However, the accuracy of estimating the invasion depth with conventional endoscopy is insufficient for determining an appropriate therapeutic method that avoids excessive surgery. In our opinion, the most reliable method for predicting invasion depth is magnified chromoendoscopy with crystal violet staining. A pit pattern classification proposed by Kudo and Tsuruta has been adopted by Japanese endoscopists.[10] Type V pit patterns, particularly the VN type pit pattern, are recognized as indications of submucosal invasion.[10] Fujii and colleagues proposed a clinical classification of invasive or non-invasive patterns, taking into account the demarcated area with irregular or distorted pits.[11] We previously reported that the invasive pattern could differentiate between intramucosal or submucosal superficial cancers (<1000 μm) and submucosal deep cancers (≥1000 μm) with sensitivity, specificity, and accuracy of 85.6%, 99.4%, and 98.8%, respectively (Fig. 1).[11] In a multivariable analysis of factors that predicted submucosal deep invasion of non-granular type LST, the invasive pattern was considered a risk factor, together with hardness and large tumor size (≥20 mm).[12] Narrow band

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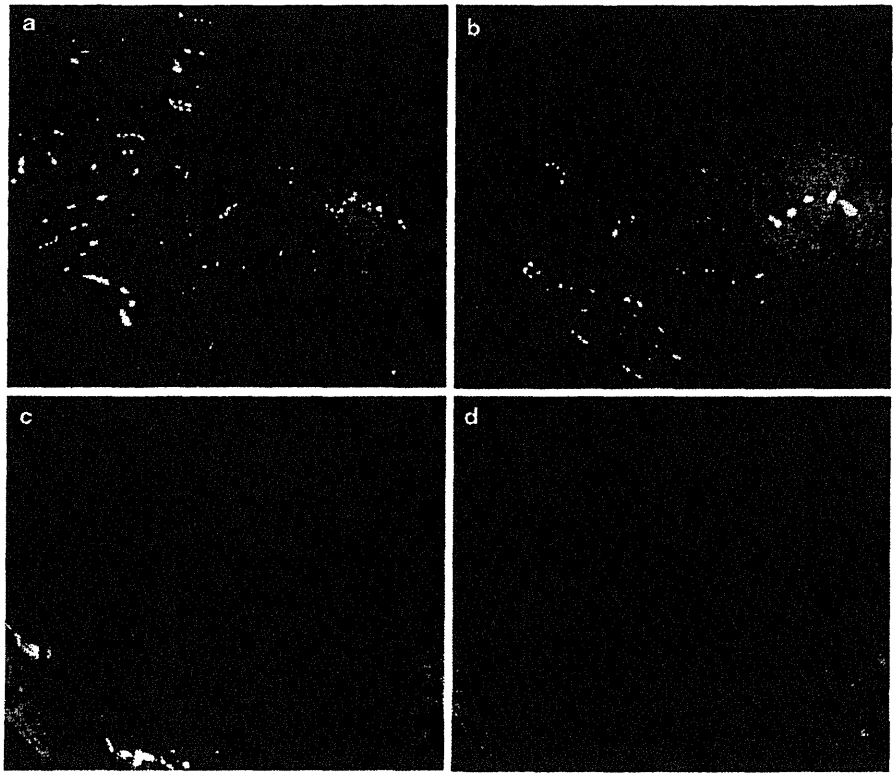

Fig. 1. A case of an invasive pattern. (a) Conventional colonoscopy showed a laterally spreading granular type tumor, with a reddish depressed area, 30 mm in diameter, in the cecum. (b) Chromoendoscopy with indigo-carmine spray dying showed a demarcated area traced by yellow dotted line. (c,d) Magnified chromoendoscopy with crystal violet staining showed invasive pattern in the demarcated area. The lesion was treated with laparoscopic surgery and pathological diagnosis was well-differentiated adenocarcinoma with submucosal invasion (2000 μm).

imaging (NBI) was recently assessed for predicting tumor invasion depth.[13] NBI offers the advantage of a simple, easy method; but currently, its diagnostic accuracy may be inferior to magnified endoscopy with crystal violet staining.[13] Endoscopic ultrasonography was also used for predicting tumor invasion depth, but it requires a higher level of skill and diagnosis is difficult, even in good conditions. Our previous controlled evaluation showed that magnified endoscopy was superior to endoscopic ultrasonography for the estimation of tumor invasion depth.[14]

SELECTION OF ENDOSCOPIC TREATMENT METHODS

The choice of endoscopic treatment methods depends on lesion size and characteristics; they include snare polypectomy, endoscopic mucosal resection (EMR), endoscopic piecemeal mucosal resection (EPMR), or endoscopic submucosal dissection (ESD). We propose that ESD is indicated for non-granular type LST (≥20 mm), due to the relatively high rates of submucosal invasion and the difficultly in predicting the invasion site prior to treatment.[15] Moreover, ESD is indicated for granular type LST, particularly mixed nodular types (≥40 mm), also due to relatively high rates of submucosal invasion.[15] Alternatively, EPMR is indicated for granular type LST (homogeneous type), due to the similarity to adenoma or intramucosal cancer. Recently, a working group for the standardization of colorectal ESD proposed that ESD is indicated for colorectal tumors with the following features: large lesions (≥20 mm in diameter) that are difficult to resect en bloc with a snare EMR, but where an endoscopic treatment is indicated; mucosal lesions with fibrosis caused by prolapse, due to biopsy or peristalsis of the lesion; sporadic localized tumors associated with chronic inflammation, e.g. ulcerative colitis; and local or residual early cancer after an endoscopic resection.[16] For pedunculated lesions, snare polypectomy of an EMR, combined with looping or clipping, is indicated when there is no endoscopic finding of stalk invasion. One controlled trial suggested that a bleeding rate was lower with combination epinephrine injection plus endoloop than epinephrine injection alone.[17]

LOCAL RECURRENCE AFTER ENDOSCOPIC RESECTION

After endoscopic resection local recurrence is an important issue in conventional EMR/EPMR methods (Fig. 2). Local recurrence rates after EPMR typically range from 10 to 23%[2,4,18–20] (Table 1). In our previous study, the local recurrence rate after a piecemeal resection was significantly higher than that after an en bloc resection, irrespective of tumor size or macroscopic features.[20] To reduce local recurrence after an EPMR, it is important to carefully note the circumferences of the edge and base of the ulcer. Magnified observation is ideal for detecting a residual tumor. Tanaka *et al.* reported that magnified observation after an EPMR could effectively reduce the local recurrence rate.[16] Argon plasma coagulation (APC) was also tested for reducing the local recurrence after EPMR. One controlled trial suggested that APC reduced the local recurrence after EPMR of large sessile tumors.[21] However, in a prospective uncontrolled study, similar recurrence rates were found with or without APC after an EPMR.[22] Thus, the usefulness of APC is controversial, but in some high-volume centers, it is routinely