

## SPECIAL REPORT

# CURRENT STATUS IN THE OCCURRENCE OF POSTOPERATIVE BLEEDING, PERFORATION AND RESIDUAL/LOCAL RECURRENCE DURING COLONOSCOPIC TREATMENT IN JAPAN

SHIRO OKA, SHINJI TANAKA, HIROYUKI KANAOKA, HIDEKI ISHIKAWA, TOSHIAKI WATANABE, MASAHIRO IGARASHI, YUTAKA SAITO, HIROAKI IKEMATSU, KIYONORI KOBAYASHI, YUJI INOUE, NAOHISA YAHAGI, SUMIO TSUDA, SEIJI SIMIZU, HIROYASU IISHI, HIROO YAMANO, SHIN-EI KUDO, OSAMU TSURUTA, SATOSHI TAMURA, YUSUKE SAITO, EISAI CHO, TAKAHIRO FUJII, YASUSHI SANO, HISASHI NAKAMURA, KENICHI SUGIHARA AND TETSUICHIRO MUTO

*Colorectal Endoscopic Resection Standardization Implementation Working Group, Japanese Society for Cancer of the Colon and Rectum, Tokyo, Japan*

Bleeding, perforation, and residual/local recurrence are the main complications associated with colonoscopic treatment of colorectal tumor. However, current status regarding the average incidence of these complications in Japan is not available. We conducted a questionnaire survey, prepared by the Colorectal Endoscopic Resection Standardization Implementation Working Group, Japanese Society for Cancer of the Colon and Rectum (JSCCR), to clarify the incidence of postoperative bleeding, perforation, and residual/local recurrence associated with colonoscopic treatment. The total incidence of postoperative bleeding was 1.2% and the incidence was 0.26% with hot biopsy, 1.3% with polypectomy, 1.4% with endoscopic mucosal resection (EMR), and 1.7% with endoscopic submucosal dissection (ESD). The total incidence of perforation was 0.74% (0.01% with the hot biopsy, 0.17% with polypectomy, 0.91% with EMR, and 3.3% with ESD). The total incidence of residual/local recurrence was 0.73% (0.007% with hot biopsy, 0.34% with polypectomy, 1.4% with EMR, and 2.3% with ESD). Colonoscopic examination was used as a surveillance method for detecting residual/local recurrence in all hospitals. The surveillance period differed among the hospitals; however, most of the hospitals reported a surveillance period of 3–6 months with mainly transabdominal ultrasonography and computed tomography in combination with the colonoscopic examination.

**Key words:** colorectal endoscopic resection, perforation, postoperative bleeding, residual/local recurrence.

## INTRODUCTION

With an increase in the number of medical examinations that are carried out for detecting colon cancer, there has also been a drastic increase in the number of colonoscopic examinations. As a result, the number of patients seeking endoscopic resection (ER) for colorectal tumor has also increased. Although surgical removal of cancer was the only option available in the past, advancements in ER procedures, including endoscopic submucosal dissection (ESD),<sup>1–7</sup> enable successful resection of early cancer. The incidences of complications, such as residual/local recurrence, after colonoscopic treatment have also been reported in a study conducted by a hospital, but not in a multicenter study involving general hospitals. In addition, each hospital adopted a different methodology for surveillance. Therefore, current trends regarding the incidence of these complications

in Japan are not available. Here, we report the results of a questionnaire survey, carried out by the Colorectal Endoscopic Resection Standardization Implementation Working Group, JSCCR (Japanese Society for Cancer of the Colon and Rectum), that examined current trends in the incidence of postoperative bleeding, perforation, residual/local recurrence, and surveillance methods used after ER, depending on the type of endoscopic procedure.

## METHODS

We gave the questionnaire to 85 586 participants across 107 hospitals (Table 1), which were part of the JSCCR, over a period of 2 years (January 2004–December 2005). We sent the questionnaire to 294 facilities which participated in the Japanese Society for Cancer of the Colon and Rectum, and the percentage of hospitals returning the questionnaire was 36.4% (107/294). The participants were questioned about the incidence of complications, such as postoperative bleeding, perforation, residual/local recurrence, and the surveillance methods used after ER, depending on the type of endoscopic procedure. The endoscopic procedures used included 14 382 lesions by hot biopsy; 34 433 lesions by polypectomy; 36 083 lesions by endoscopic mucosal resection (EMR); and 688 lesions by ESD. Postoperative bleeding was defined as

Correspondence: Shinji Tanaka, Department of Endoscopy, Hiroshima University Hospital, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan. Email: colon@hiroshima-u.ac.jp

Summary of a Multicenter Questionnaire Survey Conducted by the Colorectal Endoscopic Resection Standardization Implementation Working Group in Japanese Society for Cancer of the Colon and Rectum.

Received 11 December 2009; accepted 7 June 2010.

**Table 1.** Facilities that answered questionnaire examining current trends in the incidence of postoperative bleeding, perforation, residual/local recurrence, and surveillance methods used after ER<sup>†</sup>

First Department of Internal Medicine, Sapporo Medical University	National Cancer Center Hospital East
Fukuoka Dental College Medical and Dental Hospital	Sapporo Kosei General Hospital
Division of Gastroenterology, Kurume University School of Medicine	First Department of Surgery, Yamanashi University
Department of Gastroenterology, Fujita Health University	Asahikawa City Hospital
Yamagata University Hospital	Department of Coloproctological Surgery, Juntendo University
Nakatsu Municipal Hospital	Showa University Northern Yokohama Hospital
Department of Surgery, Kanto Rosai Hospital	Sendai Medical Center
Department of Surgery, Sano Ishikai Hospital	First Department of Surgery, School of Medicine
Chiba Cancer Center	University of Occupational and Environmental Health
Hakodata City Hospital	Japanese Red Cross Nagoya Daiichi Hospital
Keiyuukai Sapporo Hospital	Mitsubishi Mihara Hospital
Osaka Medical Center for Cancer and Cardiovascular Diseases	Saga University Hospital
Ishinomaki Municipal Hospital	Department of Surgery, School of Medicine, Tokai University
Shiga University of Medical Science	Department of Surgery, Tottori University
Haga Red Cross Hospital	Department of Surgery, Kinki University School of Medicine
NTT West Osaka Hospital	Saiseikai Niigata Daini Hospital
Department of Surgery, National Defense Medical College Hospital	Kumamoto Municipal Hospital
Showa University	Yokohama General Hospital
Saitama Medical Center Jichi Medical University	Sapporo Social Insurance General Hospital
South Miyagi Medical Center	Toyama University Hospital
Ibaraki Prefectural Central Hospital	Uwajima City Hospital
National Cancer Center Hospital	Nishi Sapporo National Hospital
Cancer Institute Hospital of Japanese Foundation for Cancer Research	Department of Gastroenterology and Hepatology, Kyoto University
First Department of Internal Medicine, Iwate Medical University	Matsunami General Hospital
First Department of Internal Medicine, Hirosaki University	Saitama Red Cross Hospital
Department of Endoscopy, Kochi Medical School	Sakai Municipal Hospital
Yaizu City Hospital	Kure City Medical Association Hospital
Osaka Central Hospital	Chikuba Hospital for Proctological and Gastrointestinal Diseases
Niigata City General Hospital	Niigata University Hospital
Hyogo College of Medicine	Kanagawa Cancer Center
National Hospital Organization Kyushu Medical Center	Division of Surgical Oncology, Tokyo Medical and Dental University
Aichi Cancer Center Hospital	Tokyo Metropolitan Tama Cancer Detection Center
Second Department of Surgery, Tokyo Women's Medical University	Mie University Hospital
Kanazawa University Hospital	Surgery for Organ Function and Biological Regulation, Nippon Medical School
Division of Surgical Oncology, Nagoya University	Department of Medicine, Division of Gastroenterology, Jichi Medical University
Yokohama City University Hospital	Nippon Medical School Chiba Hokusou Hospital
JR Osaka Railway Hospital	Nara Medical University
Kakegawa City General Hospital	Department of Surgery, Jichi Medical University
Misawa City Hospital	Akita Red Cross Hospital
Fukuya Red Cross Hospital	Showa University Toyosu Clinic
Hyogo Cancer Center	Department of Gastroenterology, Chofu Surgical Clinic
Yao Municipal Hospital	Department of Surgery, Teikyo University School of Medicine
Department of Thoracic Visceral Organ Surgery, Gunma University	Department of Gastroenterology and Hepatology, Tokyo Medical University
Saitama Cancer Center	Institute of Gastroenterology, Tokyo Women's Medical University
Hyogo College of Medicine	Gastroenterological Surgery, Toho University Medical Center Omori Hospital
Fukushima Medical University Hospital	Tohoku University Hospital
Keio University Hospital	Nihon University Itabashi Hospital
Fukuiken Saiseikai Hospital	Fukuoka University Chikushi Hospital
Iwakuni Clinical Center	Kitasato University East Hospital
Fukuoka University Chikushi Hospital	Department of Endoscopy, Hiroshima University Hospital
Sendai Kousei Hospital	Tokushima University Hospital
Asahikawa-Kousei General Hospital	Institute of Gastroenterology, Musashikosugi Hospital, Nippon Medical School
Department of Endoscopy, Kochi Medical University	

<sup>†</sup>Two hospitals were unnamed in the questionnaire. ER, endoscopic resection.

**Table 2.** Frequency of postoperative bleeding, perforation and local residue/recurrence depending on the type of endoscopic procedure

	Hot biopsy <i>n</i> = 14 382	Polypectomy <i>n</i> = 34 433	EMR <i>n</i> = 36 083	ESD <i>n</i> = 688	Total (%) <i>n</i> = 85 586
Postoperative bleeding (%)	38 (0.3)	444 (1.3)	520 (1.4)	12 (1.7)	1014 (1.2)
Requirement for surgical treatment (%)	0 (0)	1 (0.2)	1 (0.2)	0 (0)	2 (0.2)
Perforation (%)	2 (0.01)	6 (0.02)	33 (0.09)	23 (3.3)	64 (0.07)
Requirement for surgical treatment (%)	1 (5.0)	4 (66.7)	18 (54.5)	14 (60.9)	37 (57.8)
Local residue/recurrence (%)	1 (0.007)	118 (0.3)	494 (1.4)	16 (2.3)	629 (0.7)

\**P* < 0.001.

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

the condition in which the hemoglobin (Hb) content of the blood was lower than 2 g/dL or symptoms, such as hematemesis or melena, were revealed.<sup>8</sup> Perforation during the procedure was immediately sutured by clipping and confirmed by detection of free air on plain radiography or computed tomography (CT) image. Statistical analysis was carried out using the chi-squared test, with values of *P* < 0.05 considered statistically significant.

## RESULTS

### Frequency of postoperative bleeding depending on the type of endoscopic procedure

The total frequency of incidence of postoperative bleeding was 1.2% (1014/85 586). The frequencies for each endoscopic procedure used were as follows: 0.26% (38/14 382) by hot biopsy, 1.3% (444/34 433) by polypectomy, 1.4% (520/36 083) by EMR, and 1.7% (12/688) by ESD. The frequency of incidence was significantly lowest for hot biopsy as compared to the other procedures (Table 2).

Surgery of necessity for the treatment of postoperative bleeding was carried out at the rate of 0.20% (2/1014). The surgical rates depending on the type of endoscopic procedure used were 0.23% (1/444) by polypectomy and 0.19% (1/520) by EMR. Bleeding by other procedures was successfully treated by endoscopic procedures.

### Frequency of perforation depending on the type of endoscopic procedure

The total frequency of incidence of perforation was 0.74% (64/85 586). The frequencies for each endoscopic procedure

used were as follows: 0.01% (2/14 382) by hot biopsy, 0.017% (6/34 433) by polypectomy, 0.091% (33/36 083) by EMR, and 3.3% (23/688) by ESD. The frequency of incidence was significantly highest for ESD as compared to the other procedures (Table 2).

Surgery for the treatment of perforation was carried out at the rate of 57.8% (37/64). The surgical rates depending on the endoscopic procedure were as follows: 50.0% (1/2) by hot biopsy, 66.7% (4/6) by polypectomy, 54.5% (18/33) by EMR, and 60.9% (14/23) by ESD. There was no significant difference in the surgical rates among the endoscopic procedures.

### Frequency of residual/local recurrence depending on the type of endoscopic procedure

The total frequency of incidence of residual/local recurrence was 0.73% (629/85 586). The frequencies for each endoscopic procedure used were as follows: 0.007% (1/14 382) by hot biopsy, 0.34% (118/34 433) by polypectomy, 1.4% (494/36 083) by EMR, and 2.3% (16/688) by ESD. The frequencies were significantly higher for EMR and ESD than for hot biopsy and polypectomy (Table 2).

### Surveillance methods after ER

Colonoscopic examination was used as a surveillance method for detecting residual/local recurrence in all 107 hospitals. In addition, three of the hospitals separately used transabdominal ultrasound (TUS), CT, and barium enema examination in combination with colonoscopic examination. Follow-up duration from the end of ER to initial examination was  $5.7 \pm 3.2$  (range 1–12) months and that from the initial

examination to the second examination was  $12.0 \pm 6.2$  (range 2–36) months, among the 91 hospitals that had responded to the questionnaire.

Surveillance for tumor metastasis was carried out by colonoscopic examination in five hospitals (4.7%), TUS in 47 hospitals (43.9%), CT scan in 98 hospitals (91.6%), serum tumor-marker test in five hospitals (4.7%), positron-emission tomography (PET) in three hospitals (2.8%), and by chest X-ray examination in two hospitals (1.9%), among all the 107 hospitals examined. Follow-up duration for the detection of metastasis from the end of ER to initial examination was  $4.9 \pm 1.9$  (range 3–36) months and that from the initial examination to the second examination was  $9.5 \pm 3.5$  (range 3–24) months, among the 91 hospitals that had responded to the questionnaire.

## DISCUSSION

Our data revealed higher frequencies of postoperative bleeding than those reported in previous studies.<sup>9–19</sup> An increase in the number of patients with larger lesions, such as laterally spreading tumors (LST), and the increased use of ER for treating colon cancers as compared to the numbers at the time when the previous studies were published might be a reason for the higher frequencies obtained in the present study. In addition, the inclusion of ESD data might have influenced the results, although data from only a few cases of ESD were included in the present study.

Bleeding has the highest frequency among the incidences associated with colonoscopic treatment. In the frequency of postoperative bleeding, we could not observe any difference among polypectomy, EMR and ESD. However, the frequency of postoperative bleeding in hot biopsy was the lowest. Requirement for surgical treatment for postoperative bleeding was seen in only 0.2% of the cases in our study. This result shows that endoscopic techniques, such as clipping, are sufficient to arrest bleeding. Important factors in the endoscopic procedure for bleeding are the arrangement of the apparatus and drugs for maintaining bleeding, extensive experience with resection techniques, appropriate treatment for bleeding, postoperative management, preoperative examination of a patient's overall medical condition, and preoperative acquisition of informed consent. The patient's bleeding tendency and intake of antiplatelet and anticoagulant drugs are also important factors that should be considered before carrying out the surgery. Perforation, which is a rare incidence compared to postoperative bleeding, can sometimes become serious. Our study showed a result (3.3%) similar to other studies<sup>1–7,14</sup> in which the frequency of perforation by ESD was significantly higher than that with other treatment methods. ESD is difficult to carry out because the bowel has a thin wall and it exhibits flexure and peristalsis.<sup>3,20</sup> For treating perforation, proper management after treatment is very important.

At first, intestinal tension is relieved by aspirating air through the intestine, and then the perforating lesion is closed using clips. However, the requirement for surgical treatment following perforation was high, irrespective of the treatment methods used.<sup>2,3</sup>

The questionnaire study found that the frequency of residual/local recurrence after ER was 0.73%. Residual/local

recurrence may occur if the lesion is incompletely resected. Therefore, surveillance after ER becomes important. Two prospective studies have examined residual/local recurrence after ER. Higaki *et al.*<sup>21</sup> reported that the frequency of residual/local recurrence was four (four piecemeal resections) of 24 LST lesions by follow up during a 24-month-period after ER, and Hurlstone *et al.*<sup>22</sup> reported that it was 10 (two en bloc resections, eight piecemeal resections, and nine were LST-granular types) of 58 lesions with LST by follow up during a 24-month-period after ER. Other retrospective studies revealed that the frequency of residual/local recurrence was 1.1–27.3%.<sup>15,18,21–25</sup> Most reports revealed significantly higher frequency of residual/local recurrence with piecemeal resection than with en bloc resection. An exception to this observation is a report by Tanaka *et al.*<sup>26</sup> In the present study, the frequency of residual/local recurrence by EMR was found to be as low as 1.4%, although we could not analyze the details of the EMR method. The present study also found that the frequency of residual/local recurrence after ESD was as high as 2.3%. This result could arise from the fact that ESD was changed from en bloc resection to piecemeal resection for various reasons.

The results of the present multicenter questionnaire survey clearly show the current status in the incidence of postoperative bleeding, perforation, and residual/local recurrence during colonoscopic treatment in Japan. Therefore, to ensure the well-being of the patient, an endoscopist who specializes in treating colorectal tumors must be cautious enough to prevent the occurrence of such incidences, in spite of the increase in the number of ER for colorectal tumor.

## ACKNOWLEDGMENT

This study was carried out within the framework of a project undertaken by the Colorectal Endoscopic Resection Standardization Implementation Working Group, Japanese Society for Cancer of the Colon and Rectum Grants.

## REFERENCES

1. Yahagi N, Fujishiro M, Omata M. Endoscopic submucosal dissection of colorectal lesion. *Dig. Endosc.* 2004; **16** (Suppl): S178–81.
2. Tsuda S. Complications related to endoscopic submucosal dissection (ESD) of colon and rectum and risk management procedures. *Early colorectal cancer* 2006; **10**: 539–50. (in Japanese with English abstract).
3. Tanaka S, Oka S, Kaneko I *et al.* Endoscopic submucosal dissection for colorectal neoplasia: Possibility of standardization. *Gastrointest. Endosc.* 2007; **66**: 100–7.
4. Hurlstone DP, Atkinson R, Sanders DS *et al.* Achieving R0 resection in the colorectum using endoscopic submucosal dissection. *Br. J. Surg.* 2007; **94**: 536–42.
5. Fujishiro M, Yahagi N, Kakushima N *et al.* Outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms in 200 consecutive cases. *Clin. Gastroenterol. Hepatol.* 2007; **5**: 678–83.
6. Tamagi Y, Saito Y, Masaki N *et al.* Endoscopic submucosal dissection: A safe technique for colorectal tumors. *Endoscopy* 2007; **39**: 418–22.
7. Saito Y, Uraoka T, Matsuda T *et al.* Endoscopic treatment of large superficial colorectal tumors: A case series of 200 endoscopic submucosal dissections (with video). *Gastrointest. Endosc.* 2007; **66**: 966–73.



8. Tajiri H, Kitano S. Complications associated with endoscopic mucosal resection: Definition of bleeding that can be viewed as accidental. *Dig. Endosc.* 2004; **16** (Suppl): S134–36.
9. Yokota T, Sugihara K, Yoshida S. Endoscopic mucosal resection for colorectal neoplastic lesions. *Dis. Colon Rectum* 1994; **37**: 1108–11.
10. Tada M, Inoue H, Yabata E *et al.* Colonic mucosal resection using a transparent cap fitted endoscope. *Gastrointest. Endosc.* 1996; **44**: 63–5.
11. Yoshikane H, Hidano H, Sakakibara A *et al.* Endoscopic resection of laterally spreading tumors of the large intestine using a distal attachment. *Endoscopy* 1999; **31**: 426–30.
12. Rembacken BJ, Fujii T, Carins A *et al.* Flat and depressed colonoscopic neoplasms: A prospective study of 1000 colonoscopies in the UK. *Lancet* 2000; **355**: 1211–4.
13. Ahmad NA, Kochman ML, Long WB *et al.* Efficacy, safety, and clinical outcomes of endoscopic mucosal resection: A study of 101 cases. *Gastrointest. Endosc.* 2001; **55**: 390–6.
14. Mena F, De Vogelaere K, Uraban D *et al.* Iatrogenic perforation of the colon during diagnostic colonoscopy: Endoscopic treatment with clips. *Gastrointest. Endosc.* 2001; **54**: 258–9.
15. Tanaka S, Haruma K, Oka S *et al.* Clinicopathologic features and endoscopic treatment of superficially spreading colorectal neoplasms larger than 20 mm. *Gastrointest. Endosc.* 2001; **54**: 62–6.
16. Bergmann U, Beger HG. Endoscopic mucosal resection for advanced non-polypoid colorectal adenoma and early stage carcinoma. *Surg. Endosc.* 2003; **17**: 475–9.
17. Conio M, Repici A, Demarquay JF *et al.* EMR of large sessile colorectal polyps. *Gastrointest. Endosc.* 2004; **60**: 234–41.
18. Tamura S, Nakajo K, Yokoyama Y *et al.* Evaluation of endoscopic mucosal resection for laterally spreading rectal tumors. *Endoscopy* 2004; **36**: 306–12.
19. Bories E, Pesenti C, Monges G *et al.* Endoscopic mucosal resection for advanced sessile adenoma and early-stage colorectal carcinoma. *Endoscopy* 2006; **38**: 231–5.
20. Oka S, Tanaka S, Kaneko I *et al.* Techniques and pitfalls of endoscopic submucosal dissection for colorectal tumors. *Digestion* 2007; **19** (Suppl): S30–3.
21. Higaki S, Hashimoto S, Harada K *et al.* Long-term follow-up of large flat colorectal tumors resected endoscopically. *Endoscopy* 2003; **35**: 845–9.
22. Hurlstone DP, Sanders DS, Cross SS *et al.* Colonoscopic resection of lateral spreading tumours: A prospective analysis of endoscopic mucosal resection. *Gut* 2004; **53**: 1334–9.
23. Walsh RM, Ackroyd FW, Shellito PC. Endoscopic resection of large sessile colorectal polyps. *Gastrointest. Endosc.* 1992; **38**: 303–9.
24. Binmoeller KF, Bohnacker S, Seifert H *et al.* Endoscopic snare excision of 'giant' colorectal polyps. *Gastrointest. Endosc.* 1996; **43**: 183–8.
25. Zlatanovic J, Waye JD, Kim PS *et al.* Large sessile colonic adenomas: Use of argon plasma coagulator to supplement piecemeal snare polypectomy. *Gastrointest. Endosc.* 1999; **49**: 731–5.
26. Tanaka S, Oka S, Chayama K *et al.* Knack and practical technique of colonoscopic treatment focused on endoscopic mucosal resection using snare. *Dig. Endosc.* 2009; **21** (Suppl): S38–42.