

Received: 2018.02.06  
Accepted: 2018.04.09  
Published: 2018.09.29

# Endoscopic Submucosal Dissection Decreases Additional Colorectal Resection for T1 Colorectal Cancer

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ABCDEF 1 **Yuichi Tomiki**  
B 1 **Masaya Kawai**  
B 1 **Shingo Kawano**  
AB 1 **Shun Ishiyama**  
ACD 1 **Kiichi Sugimoto**  
B 1 **Makoto Takahashi**  
C 1 **Yutaka Kojima**  
B 2 **Takashi Murakami**  
B 2 **Hideaki Ritsuno**  
BE 2 **Tomoyoshi Shibuya**  
ABF 2 **Naoto Sakamoto**  
ACDEF 1 **Kazuhiro Sakamoto**

1 Department of Coloproctological Surgery, Juntendo University, Faculty of Medicine, Tokyo, Japan  
2 Department of Gastroenterology, Juntendo University, Faculty of Medicine, Tokyo, Japan

**Corresponding Author:** Yuichi Tomiki, e-mail: tomiki@juntendo.ac.jp  
**Source of support:** Departmental sources

**Background:** There are 3 methods of treating T1 colorectal cancer (T1 CRC), which include endoscopic resection, endoscopic resection followed by additional colorectal resection, and surgical resection. In this retrospective study, changes in the management of T1 CRC after introduction of endoscopic submucosal dissection (ESD) were investigated by comparison with the 10-year period before introduction of ESD.





**Material/Methods:** During a 20-year period from 1996 to 2015, 835 patients with T1 CRC were treated, including 331 patients before introduction of ESD (Group A) and 504 patients after introduction of ESD (Group B). Clinicopathological findings and treatment methods were compared between these 2 groups.

**Results:** As the initial treatment, endoscopic treatment was performed in 185 patients (55.9%) in Group A and 288 (57.1%) in Group B. In Group B, ESD was performed in 161 patients (55.9%), accounting for more than half of the T1 CRC patients receiving endoscopic treatment. In Groups A and B, observation after endoscopic resection was selected for 54.2% and 67.3% of T1a patients, respectively ( $p=0.04$ ). A similar trend was noted for T1b patients, and there was no significant difference of the treatment approach. Among all T1 CRC patients, the percentage undergoing observation after endoscopic resection was significantly higher in Group B than in Group A (34.3% vs. 26.9%,  $p=0.02$ ), and the percentage of patients undergoing additional colorectal resection was significantly lower in Group B (22.8% vs. 29.0%,  $p=0.04$ ).

**Conclusions:** After introduction of ESD, it was performed in more than half of all patients with T1 CRC undergoing endoscopic treatment. The percentage of patients undergoing observation following endoscopic resection of T1 CRC increased after introduction of ESD.

**MeSH Keywords:** **Colorectal Neoplasms • Endoscopy, Gastrointestinal • Lymphatic Metastasis**

**Full-text PDF:** <https://www.medscimonit.com/abstract/index/idArt/909380>

 2902  6  —  27



## Background

T1 colorectal cancer (T1 CRC) is invasive and can cause lymph node and distant metastases, so standard treatment involves colorectal resection combined with lymph node dissection [1–3]. However, endoscopic resection is often performed as initial treatment for T1 CRC, followed by additional colorectal resection when histopathological examination reveals a high risk of lymph node metastasis [4,5]. Thus, there are 3 treatment approaches to T1 CRC: endoscopic resection alone, endoscopic resection followed by additional colorectal resection, and standard surgical resection.

Lymph node metastasis occurs in 6–12% of patients with T1 CRC [6–8], and the depth of submucosal invasion, histological type, lymphovascular invasion, and tumor budding have been reported as risk factors for nodal metastasis [9–11]. Selection of endoscopic or surgical resection for T1 CRC is based on preoperative endoscopic diagnosis. However, the histology of the deepest invading part of the tumor, lymphovascular invasion, and tumor budding cannot be examined by preoperative endoscopy, which means that the risk of lymph node metastasis is inevitably decided by assessing the depth of submucosal invasion. In Japan, submucosal invasion shallower than 1000  $\mu\text{m}$  is classified as T1a and invasion of 1000  $\mu\text{m}$  or deeper is designated as T1b [4], with T1b representing deep submucosal invasion, which is a risk factor for lymph node metastasis. When the risk of lymph node metastasis is judged to be low based on the results of histopathological examination after endoscopic resection, observation without additional colorectal resection is selected for subsequent management [12]. Additional colorectal resection is usually recommended even if only 1 risk factor for lymph node metastasis is found [4], but observation without resection despite the presence of a risk factor for nodal metastasis is increasingly selected based on the patient's age, general condition, and wishes.

Additional colorectal resection is often performed by laparoscopic surgery, but endoscopic treatment is even less invasive. With recent progress in endoscopic treatment, endoscopic submucosal dissection (ESD) has been performed for T1 CRC in addition to endoscopic mucosal resection (EMR) [13,14]. ESD is an excellent method that allows *en-bloc* resection of even large lesions and accurate histopathological evaluation for determination of subsequent treatment options.

During the 10-year period since introduction of ESD at our hospital, the number of patients with T1 CRC undergoing ESD has increased. Accordingly, this retrospective study was performed to assess changes in the management of T1 CRC after introduction of ESD by comparing it with the 10-year period before its introduction.

## Material and Methods

### Patient involvement

During the 20-year period from 1996 to 2015, 935 patients with T1 CRC were treated at Juntendo University Hospital (Tokyo, Japan). After excluding 85 patients who underwent previous endoscopic resection at another hospital and 15 patients with synchronous multiple cancer and advanced colorectal cancer as the other tumor, 835 patients were studied.

Selection of endoscopic or surgical resection for colorectal lesion was based on preoperative endoscopic diagnosis by magnifying chromoendoscopy. For lesions with definitely suspected submucosal invasion, surgery was selected after biopsy. For lesions without submucosal invasion or with shallow invasion, endoscopic treatment was selected, and whether additional colorectal resection was necessary was determined by histological evaluation.

Written informed consent for treatment was obtained from all patients before treatment.

The 835 patients were divided into 331 patients treated between 1996 and 2005 before introduction of ESD (Group A) and 504 patients treated between 2006 and 2015 after introduction of ESD (Group B). Clinicopathological findings and treatment methods were compared between the 2 groups.

### Risk of lymph node metastasis

The risk of lymph node metastasis was judged according to the 2014 guidelines for colorectal cancer treatment [4]. Briefly, tumors with a positive vertical margin, depth of submucosal invasion  $\geq 1000$   $\mu\text{m}$ , lymphovascular invasion, poorly differentiated adenocarcinoma, signet ring cell carcinoma, mucinous carcinoma, or tumor budding (Grade 2/3) were regarded as high risk for lymph node metastasis, while tumors without any risk factors were regarded as low risk. If submucosal invasion was not measured in the earlier cases, the submucosal layer was divided into equal thirds (SM1, SM2, and SM3), with invasion into the upper third of the submucosa being classified as T1a and invasion of the middle or lower thirds being classified as T1b [15].

### Colorectal ESD

The indications for colorectal ESD specified by the Colorectal ESD Standardization Implementation Working Group and Colorectal ESD/EMR Guidelines established by the Japan Gastroenterological Endoscopy Society were followed, i.e., tumors 20 mm or larger requiring endoscopic *en-bloc* resection. Colorectal ESD was also performed for tumors smaller than

**Table 1.** Profile of T1 CRC patients.

	Group A (1996–2005)	Group B (2006–2015)	P-value
Cases	331	504	
Age, mean $\pm$ SD years	62.2 $\pm$ 11.7	66.8 $\pm$ 10.5	ns
Sex (M: F)	229 :102	313 :191	0.04
Tumor location, n (%)			
Cecum	8 (2.4%)	34 (6.8%)	<0.01
Ascending	36 (10.9%)	69 (13.7%)	ns
Transverse	37 (11.2%)	54 (10.7%)	ns
Descending	23 (6.9%)	29 (5.8%)	ns
Sigmoid	123 (37.2%)	164 (32.5%)	ns
Rectosigmoid	37 (11.2%)	42 (8.3%)	ns
Rectum above	40 (12.1%)	63 (12.5%)	ns
Rectum below	27 (8.1%)	49 (9.7%)	ns
Tumor size, mean $\pm$ SD, mm	15.6 $\pm$ 9.6	22.6 $\pm$ 15.5	<0.01
Tumor morphology, n (%)			
Pedunculated (Ip, lsp)	146 (44.1%)	133 (26.4%)	<0.01
Sessile (ls)	84 (25.4%)	100 (19.8%)	ns
Flat (IIa)	22 (6.6%)	33 (6.6%)	ns
Depressed (IIc, IIa+IIc)	39 (11.8%)	127 (25.2%)	<0.01
Laterally spreading tumor	40 (12.1%)	111 (22.0%)	<0.01
Submucosal invasion depth			
T1a (<1000 $\mu$ m)	96 (29.0%)	150 (29.8%)	ns
T1b ( $\geq$ 1000 $\mu$ m)	235 (71.0%)	354 (70.2%)	ns
Histopathological risk of lymph node metastasis			
Low-risk	72 (21.8%)	113 (22.4%)	ns
High-risk	259 (78.2%)	391 (77.6%)	ns

20 mm if *en-bloc* resection using a normal snare was difficult [16].

### Statistical analysis

Results are reported as the mean  $\pm$ SD (range). Statistical analysis was performed with JMP 9.0 software (SAS Institute Inc., Cary, NC, USA) using the chi-square test and the *t* test. The level of significance was set at  $p < 0.05$  in all analyses.

## Results

### Profile of T1 CRC patients

Group B (n=504) was 1.5-fold larger than Group A (n=331). The mean age was not significantly different, but the percentage of female patients was higher in Group B ( $p=0.04$ ). Regarding tumor location, cecal lesion increased from 2.4% to 6.8% in Group B ( $p < 0.01$ ), and the mean tumor size increased from 15.6 to 22.6 mm. Regarding the macroscopic type, pedunculated tumors showed a decrease in frequency, whereas depressed and laterally spreading tumors (LST) were increased

**Table 2.** Initial treatment.

	Group A (1996–2005)	Group B (2006–2015)	P-value
T1a	96	150	
Endoscopic resection	69 (71.9%)	120 (80.0%)	ns
Standard surgical resection	27 (28.1%)	30 (20.0%)	
T1b	235	354	
Endoscopic resection	116 (49.4%)	168 (47.5%)	ns
Standard surgical resection	119 (50.6%)	186 (52.5%)	
Total	331	504	
Endoscopic resection	185 (55.9%)	288 (57.1%)	ns
Standard surgical resection	146 (44.1%)	216 (42.9%)	

**Table 3.** Endoscopic treatment.

	Group A (1996–2005) n=185	Group B (2006–2015) n=288	P-value
Endoscopic polypectomy	64 (34.6%)	26 (9.0%)	<0.01
EMR	121 (65.4%)	101 (35.1%)	<0.01
ESD	–	161 (55.9%)	
Rate of <i>en-bloc</i> resection, n(%)	158 (85.4%)	257 (89.2%)	ns

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

in Group B. The depth of submucosal invasion was T1a in 29.0% of Group A and 29.8% of Group B, while it was T1b in 71.0% and 70.2%, respectively, showing no differences. The risk of lymph node metastasis was classified as low in 21.8% of Group A and 22.4% of Group B, while it was high in 78.2% and 77.6%, respectively, also exhibiting no differences (Table 1).

### Initial treatment

Endoscopic resection was often selected for initial treatment of T1a CRC. The endoscopic resection rate was 71.9% in Group A and it increased to 80.0% in Group B, while selection of standard surgical resection for initial treatment of T1a CRC decreased from 28.1% to 20.0%, respectively.

Selection of endoscopic resection or standard surgical resection for initial treatment of T1b CRC was similar in both groups, with endoscopic resection being selected in 49.4% of Group A and 47.5% of Group B, while standard surgical resection was selected in 50.6% and 52.5%, respectively.

Overall, endoscopic resection was performed more frequently than standard surgical resection as initial treatment in both groups (Group A: 55.9 vs. 44.1%, Group B: 57.1 vs. 42.9%), and no significant change in management was noted (Table 2).

### Endoscopic treatment

In Group A, endoscopic polypectomy was performed for 64 patients (34.6%) and EMR was performed for 121 patients (65.4%), whereas endoscopic polypectomy and EMR were respectively performed for 26 patients (9.0%) and 101 patients (35.1%) in Group B, demonstrating significant decreases in frequency ( $p < 0.01$ ). In Group B, ESD was performed for 161 patients (55.9%), accounting for more than half of the patients with T1 CRC undergoing endoscopic treatment. There was no significant difference of the *en-bloc* resection rate between Groups A and B (Table 3).

### Additional colorectal resection or observation

The risk of lymph node metastasis was judged to be high by histopathological examination after endoscopic treatment in

**Table 4.** Additional colorectal resection or observation.

	Group A (1996–2005)	Group B (2006–2015)	P-value
	n=136	n=196	
Additional colorectal resection	96 (70.6%)	115 (58.7%)	0.03
Observation	40 (29.4%)	81 (41.3%)	
Reason for selecting observation (including multiple answers)			
Patient's request	13	27	
Advanced age	12	15	
High-risk surgical patient	17	14	
Poor performance status	7	9	
Refusal colostomy	4	7	
Unfavorable risk factor was only submucosal invasion depth	18	32	

136 patients from Group A and 196 patients from Group B, and 96 patients (70.6%) and 115 patients (58.7%) received additional colorectal resection, respectively. The rate of additional resection decreased in Group B and there was a significant increase of observation without additional resection (81 patients (41.3%) in Group B versus 40 patients (29.4%) in Group A,  $p=0.03$ ).

The most frequent reason for selecting observation was the patient's request, while the patient's age, colostomy, and surgical risk due to the presence of complications were also taken into consideration. In some patients, observation was selected because the depth of submucosal invasion was the only histopathological risk factor for lymph node metastasis, and the risk was judged to be low clinically (Table 4).

### Surgical treatment

Among patients who underwent initial surgery, open laparotomy was performed in 61.6% of those from Group A versus laparoscopic surgery in 31.3%, whereas laparoscopic surgery was performed in 86.1% of these patients from Group B and open laparotomy decreased to 11.6%. Among patients undergoing additional colorectal resection, the laparoscopic surgery rate also increased from 63.5% in Group A to 87.8% in Group B.

Thus, surgical treatment (including additional colorectal resection) involved open laparotomy in 51.7% of Group A, but this decreased to 11.8% in Group B ( $p<0.01$ ), while laparoscopic surgery increased to 86.7% in Group B ( $p<0.01$ ). No difference was noted for transanal surgery.

The lymph node metastasis rate among the patients undergoing initial surgery was 7.5% in Group A and 8.8% in Group B, while it was 9.4 and 10.4%, respectively, among the patients who underwent additional colorectal resection, and it was 8.3% and 9.4%, respectively, among all patients. These rates showed no significant differences (Table 5). The overall lymph node metastasis rates in all patients, including those treated by endoscopic resection, was 6.0% in Groups A and 6.2% in Group B.

### Definitive treatment

Observation was selected after endoscopic resection for 54.2% of T1a patients in Group A and 67.3% in Group B, with a significant increase in Group B ( $p=0.04$ ). A similar trend was noted among T1b patients, but there was no significant difference of the treatment method. Among all T1 CRC patients, the percentage undergoing observation after endoscopic resection increased significantly from 26.9% in Group A to 34.3% in Group B ( $p=0.02$ ), while the percentage of patients receiving surgical resection decreased from 73.1% to 65.7%, respectively. In particular, the percentage of patients receiving additional colorectal resection decreased significantly from 29.0% in Group A to 22.8% in Group B ( $p=0.04$ ). The percentage of patients undergoing initial surgical resection was 44.1% and 42.9%, respectively, showing no change (Table 6).

### Discussion

Treatment of colorectal cancer has recently undergone major changes with progress in endoscopic and laparoscopic surgery, as well as new chemotherapy regimens based on novel anticancer drugs [4,17]. Minimally invasive treatments have become

**Table 5.** Surgical treatment.

	Group A (1996–2005)	Group B (2006–2015)	P-value
Standard surgical resection	146	216	
Open surgery	90 (61.6%)	25 (11.6%)	<0.01
Laparoscopic surgery	53 (36.3%)	186 (86.1%)	<0.01
Transanal surgery	3 (2.1%)	5 (2.3%)	ns
Lymph node metastasis	11 (7.5%)	19 (8.8%)	ns
Additional colorectal resection	96	115	
Open surgery	35 (36.5%)	14 (12.2%)	<0.01
Laparoscopic surgery	61 (63.5%)	101 (87.8%)	<0.01
Lymph node metastasis	9 (9.4%)	12 (10.4%)	ns
Total	242	331	
Open surgery	125 (51.7%)	39 (11.8%)	<0.01
Laparoscopic surgery	114 (47.1%)	287 (86.7%)	<0.01
Transanal surgery	3 (1.2%)	5 (1.5%)	ns
Lymph node metastasis	20 (8.3%)	31 (9.4%)	ns

**Table 6.** Definitive treatment.

	Group A (1996–2005)	Group B (2006–2015)	P-value
T1a	96	150	
Endoscopic resection	52 (54.2%)	101 (67.3%)	0.04
Additional colorectal resection	17 (17.7%)	19 (12.7%)	ns
Standard surgical resection	27 (28.1%)	30 (20.0%)	ns
T1b	235	354	
Endoscopic resection	37 (15.7%)	72 (20.3%)	ns
Additional colorectal resection	79 (33.6%)	96 (27.1%)	ns
Standard surgical resection	119 (50.6%)	186 (52.6%)	ns
Total	331	504	
Endoscopic resection	89 (26.9%)	173 (34.3%)	0.02
Additional colorectal resection	96 (29.0%)	115 (22.8%)	0.04
Standard surgical resection	146 (44.1%)	216 (42.9%)	ns

mainstream, and ESD has been attracting attention [18]. In this study, changes in the management of T1 CRC after the introduction of ESD were investigated.

Comparison between before and after introduction of ESD showed a 1.5-fold increase of T1 CRC in the 10-year period after its introduction, which may have reflected increased early

detection of colorectal cancer in Japan thanks to progress in endoscopy. In addition, the percentage of female colorectal cancer patients and patients with cecal lesion increased. Regarding the macroscopic type, pedunculated tumors decreased, while depressed tumors and LST increased. The tumor diameter also increased as LST increased, but there was no change in the depth of submucosal invasion or the percentages of T1a and

T1b tumors when the borderline was set at 1000  $\mu\text{m}$ . In addition, there was no change in the percentages of patients with a low or high risk of lymph node metastasis.

There are 3 treatment approaches for T1 CRC: endoscopic resection, endoscopic resection followed by additional colorectal resection, and standard surgical resection. Considering that T1 CRC is an invasive tumor with a risk of lymph node metastasis and high-risk patients account for approximately 80%, surgery with lymph node dissection is the standard treatment approach [1–3]. However, endoscopic resection is often performed initially because complete cure of some lesions by endoscopic treatment is expected if lymph node metastasis is absent in T1 CRC, and a strategy of employing endoscopic resection as total excisional biopsy to investigate the need for additional colorectal resection is described in the guidelines [4]. Indeed, endoscopic resection was performed as the initial treatment for T1 CRC in 55.9% of patients during the 10-year period before introduction of ESD, although this increased to 73.1% of patients when those receiving additional colorectal resection after endoscopic resection were combined with those having initial surgery, demonstrating that surgical resection was the main treatment for T1 CRC. Due to the subsequent introduction of ESD, the range of endoscopically resectable lesions has expanded. In addition, even among patients with high-risk disease detected by histopathological examination after endoscopic resection, there has been an increase of performing observation without additional colorectal resection. Thus, although surgical resection is still the main treatment for T1 CRC, a gradual change is evident.

After the introduction of ESD, this study showed that the percentage of T1a patients undergoing initial surgical resection decreased from 28.1% to 20.0%. In T1a patients with a low risk of lymph node metastasis, initial surgical resection should be avoided if possible. Since T1CRC is an invasive tumor despite its low risk, surgery is not considered to be over-treatment. However, it is important to have the option to select endoscopic resection as initial treatment for T1a disease.

There was also an increase in the number of patients undergoing observation after endoscopic resection, indicating that endoscopic resection contributed to reducing the mental, physical, and financial burden on patients. Whether or not to have additional colorectal resection is finally decided by the patient, but providing accurate information is important for making the best decision. A negative margin after *en-bloc* resection (not piecemeal resection) is desirable, and ESD will probably become the main endoscopic treatment for T1 CRC in the future [13,19]. The present study showed that ESD was selected in more than half of all endoscopic procedures for T1 CRC, substituting for polypectomy and EMR.

With regard to additional colorectal resection, the percentage of patients undergoing observation without additional resection after endoscopic resection despite being high-risk on histopathological examination increased from 29.4% to 41.3% following introduction of ESD. This may have been related to an increase in the number of patients who decided that not receiving additional colorectal resection was more beneficial after understanding the risk of recurrence [20], including those who selected observation due to the risk of surgery even though they wanted additional treatment. Reasons for the increase in patients in whom observation is selected following endoscopic resection are that local recurrence can be detected early by image enhancing endoscopy (IEE) with magnification, and the accuracy of not only endoscopy, but also other imaging techniques, such as multi-slice CT, has increased, which allows rapid management for recurrence after endoscopic resection [21].

Minimally invasive laparoscopic surgery is often performed for additional colorectal resection, but surgical stress and complications may reduce postoperative QOL and can even be life-threatening [20,22]. Colostomy is not well understood [23]. Although many patients selected it in this study, among patients for whom surgery was high risk and postoperative reduction of QOL was a concern, the frequency of selecting observation without additional colorectal resection increased in relation to their age, complications, and performance status. The numbers of patients with a poor performance status and complications for whom it is difficult to decide about additional treatment will probably increase in the future. In addition, some patients with deep submucosal invasion as the only risk factor for lymph node metastasis were judged to be low risk clinically and were managed by observation because their risk of recurrence is low [24,25]. While T1b CRC is classified as high risk, the factors associated with a low risk of lymph node metastasis have been investigated [19,20,26], and the indications for observation without additional colorectal resection may be expanded by combining several factors.

Surgical resection is performed laparoscopically in nearly 90% of patients and T1 CRC is particularly suitable for laparoscopic surgery [27]. The lymph node metastasis rate in surgically treated patients, combining those who received additional colorectal resection and those with initial surgery, was nearly 10% in this series, as previously reported [6–8]. Adding the patients who underwent endoscopic resection, who were regarded as not having lymph node metastasis, the lymph node metastasis rate for all T1 CRC patients was approximately 6%.

Regarding definitive treatment, patients who received endoscopic resection increased and patients who received additional colorectal resection decreased as observation was increasingly selected following endoscopic resection. Although surgical resection remains the main treatment for T1 CRC, the surgical

and endoscopic resection rates changed from 73.1% vs. 26.9% (3: 1) in Group A to 65.7% vs. 34.3% (2: 1) in Group B, and these changes may have been related to introduction of ESD.

Several limitations of this study should be considered. Although ESD has become more popular, it is still not a general treatment and the data were collected at an institution where ESD is actively performed. Thus, it is necessary to investigate the impact of ESD at multiple institutions. In addition, this study presented short-term outcomes following changes in the treatment of T1 CRC, and further investigation is necessary to assess recurrence in patients who selected observation without additional colorectal resection.

## Conclusions

Changes in the treatment of T1 CRC after introduction of ESD were investigated. After ESD was introduced, it was used for

tumor resection in more than half of the endoscopically treated patients with T1 CRC. The percentage of patients managed by observation after endoscopic resection increased after introduction of ESD, not only because of its introduction, but also due to the rapid advances in endoscopy, which make *in situ* recurrence more likely to be detected and observation after endoscopic resection safer. Accordingly, there was an increased number of patients not receiving additional colorectal resection after endoscopic resection, even though they were at high risk according to histopathological examination. In the future, it will be necessary to standardize the ESD procedure for safe application and to carefully follow high-risk patients who selected observation in order to determine the clinical course, recurrence rate, and outcomes.

## Conflicts of interest

None.

## References:

1. Christie JP: Malignant colon polyps – cure by colonoscopy or colectomy? *Am J Gastroenterol*, 1984; 79: 543–47
2. Saitoh Y, Inaba Y, Sasaki T et al: Management of colorectal T1 carcinoma treated by endoscopic resection. *Dig Endosc*, 2016; 28: 324–29
3. Iida S, Hasegawa H, Okabayashi K et al: Risk factors for postoperative recurrence in patients with pathologically T1 colorectal cancer. *World J Surg*, 2012; 36: 424–30
4. Watanabe T, Itabashi M, Shimada Y et al: Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. *Int J Clin Oncol*, 2015; 20: 207–39
5. Nozawa H, Ishihara S, Fujishiro M et al: Outcome of salvage surgery for colorectal cancer initially treated by upfront endoscopic therapy. *Surgery*, 2016; 159: 713–20
6. Wang HS, Liang WY, Lin TC et al: Curative resection of T1 colorectal carcinoma: Risk of lymph node metastasis and long-term prognosis. *Dis Colon Rectum*, 2005; 48: 1182–92
7. Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR: Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. *Dis Colon Rectum*, 2002; 45: 200–6
8. Yamamoto S, Watanabe M, Hasegawa H et al: The risk of lymph node metastasis in T1 colorectal carcinoma. *Hepatogastroenterology*, 2004; 51: 998–1000
9. Ueno H, Mochizuki H, Hashiguchi Y et al: Risk factors for an adverse outcome in early invasive colorectal carcinoma. *Gastroenterology*, 2004; 127: 385–94
10. Suh JH, Han KS, Kim BC et al: Predictors for lymph node metastasis in T1 colorectal cancer. *Endoscopy*, 2012; 44: 590–95
11. Tateishi Y, Nakanishi Y, Taniguchi H et al: Pathological prognostic factors predicting lymph node metastasis in submucosal invasive (T1) colorectal carcinoma. *Mod Pathol*, 2010; 23: 1068–72
12. Yoda Y, Ikematsu H, Matsuda T et al: A large-scale multicenter study of long-term outcomes after endoscopic resection for submucosal invasive colorectal cancer. *Endoscopy*, 2013; 45: 718–24
13. Asayama N, Oka S, Tanaka S et al: Endoscopic submucosal dissection as total excisional biopsy for clinical T1 colorectal carcinoma. *Digestion*, 2015; 91: 64–69
14. Overwater A, Kessels K, Elias SG et al: Endoscopic resection of high-risk T1 colorectal carcinoma prior to surgical resection has no adverse effect on long-term outcomes. *Gut*, 2018; 67: 284–90
15. Kudo S: Endoscopic mucosal resection of flat and depressed types of early colorectal cancer. *Endoscopy*, 1993; 25: 455–61
16. Tanaka S, Tamegai Y, Tsuda S et al: Multicenter questionnaire survey on the current situation of colorectal endoscopic submucosal dissection in Japan. *Dig Endosc*, 2010; 22: S2–8
17. Bartel MJ, Brahmabhatt BS, Wallace MB: Management of colorectal T1 carcinoma treated by endoscopic resection from the Western perspective. *Dig Endosc*, 2016; 28: 330–41
18. Tanaka S, Oka S, Chayama K: Colorectal endoscopic submucosal dissection: Present status and future perspective, including its differentiation from endoscopic mucosal resection. *J Gastroenterol*, 2008; 43: 641–51
19. Saito Y, Fukuzawa M, Matsuda T et al: Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. *Surg Endosc*, 2010; 24: 343–52
20. Benizri El, Bereder JM, Rahili A et al: Additional colectomy after colonoscopic polypectomy for T1 colon cancer: a fine balance between oncologic benefit and operative risk. *Int J Colorectal Dis*, 2012; 27: 1473–78
21. Bai RJ, Ren SH, Jiang HJ et al: Accuracy of multi-slice spiral computed tomography for preoperative tumor node metastasis (TNM) staging of colorectal carcinoma. *Med Sci Monit*, 2017; 23: 3470–79
22. Cabilan CJ, Hines S: The short-term impact of colorectal cancer treatment on physical activity, functional status and quality of life: A systematic review. *JBI Database System Rev Implement Rep*, 2017; 15: 517–66
23. Katsuno H, Maeda K, Hanai T et al: Current status of local treatment for early rectal cancer in Japan: A questionnaire survey by the 81<sup>st</sup> Congress of the Japanese Society for Cancer of the Colon and Rectum (JSCCR) in 2014. *Int J Clin Oncol*, 2016; 21: 320–28
24. Nakadoi K, Tanaka S, Kanao H et al: Management of T1 colorectal carcinoma with special reference to criteria for curative endoscopic resection. *J Gastroenterol Hepatol*, 2012; 27: 1057–62
25. Yoshii S, Nojima M, Noshio K et al: Factors associated with risk for colorectal cancer recurrence after endoscopic resection of T1 tumors. *Clin Gastroenterol Hepatol*, 2014; 12: 292–302
26. Takatsu Y, Fukunaga Y, Hamasaki S et al: Recurrent colorectal cancer after endoscopic resection when additional surgery was recommended. *World J Gastroenterol*, 2016; 22: 2336–41
27. Veldkamp R, Kuhry E, Hop WC et al: Laparoscopic surgery versus open surgery for colon cancer: Short-term outcomes of a randomised trial. *Lancet Oncol*, 2005; 6: 477–84