Viszeralmedizin
Gastrointestinal Medicine and Surgery

Review Article · Übersichtsarbeit

Viszeralmedizin 2014;30:39–44
DOI: 10.1159/000358529

Published online: February 3, 2014

Endoscopic Submucosal Dissection (ESD) in Colorectal Tumors

Franz Ludwig Dumoulin[a] Bernd Sido[b] Reinhard Bollmann[c] Malte Sauer[a]

[a] Department of Medicine and Gastroenterology,
[b] Department of General and Abdominal Surgery, Gemeinschaftskrankenhaus Bonn,
[c] Institute for Pathology Bonn-Duisdorf, Bonn, Germany

Keywords
Endoscopic submucosal dissection · Colorectal adenoma · Early colorectal cancer · En bloc resection · Perforation · Bleeding

Summary
Background: Endoscopic submucosal dissection (ESD) – initially developed for the treatment of early gastric cancer in Japan – is an attractive option for en bloc resection of larger sessile or flat colorectal neoplasia. **Methods:** A review of the current literature on colorectal ESD was carried out. **Results:** In contrast to conventional endoscopic mucosal resection (EMR), ESD for larger colorectal neoplasia yields high en bloc resection rates and very low recurrence rates. The frequency of delayed bleeding is similar for EMR and ESD. Higher perforation rates during ESD are mostly due to microperforations identified and treated during the intervention, and are therefore of minor clinical relevance. A major disadvantage of ESD is the necessity for high-level endoscopic skills and long procedure times. ESD also has the potential to replace laparoscopic surgery or transanal endoscopic microsurgery mainly due to its lower complication rates. **Conclusion:** ESD for the resection of larger flat or sessile colorectal lesions has potential advantages over conventional EMR or minimally invasive surgery. Due to the low incidence of early gastric cancer, experience with ESD will remain limited in Western countries. The spread of colorectal ESD will depend on adequate training opportunities and also on modifications yielding a reduction in procedure time.

Schlüsselwörter
Endoskopische Submukosadissektion · Kolorektale Adenome · Kolorektale Frühkarzinome · En-bloc-Resektion · Perforation · Nachblutung

Zusammenfassung
Hintergrund: Die endoskopische Submukosadissektion (ESD) wurde zur Therapie des Magenfrühkarzinoms in Japan entwickelt. Sie ist auch eine attraktive Methode zur En-bloc-Resektion größerer sessiler oder flacher kolorektaler Adenome. **Methoden:** In dieser Übersicht wurde die Literatur zur kolorektalen ESD gesichtet und bewertet. **Ergebnisse:** Im Gegensatz zur konventionellen endoskopischen Mukosaresektion (EMR) ermöglicht die ESD eine deutlich höhere En-bloc-Resektionsrate und weist eine geringere Rezidivrate auf. Die Anzahl der Blutungskomplikationen unterscheidet sich nicht. Die höhere Perforationsrate ist von geringer klinischer Bedeutung, da es sich meist um Mikroperforationen handelt, die bei der ESD erkannt und therapiert werden. Der wesentliche Nachteil der ESD besteht in der deutlich längeren Interventionszeit. Gegenüber minimalinvasiven chirurgischen Therapieformen weist die ESD den Vorteil der geringeren Komplikationsrate auf. **Schlussfolgerungen:** Die kolorektale ESD hat Vorteile gegenüber der konventionellen EMR und auch gegenüber der minimalinvasiven Chirurgie. Aufgrund der geringen Inzidenz des Magenfrühkarzinoms wird die Erfahrung mit ESD in den westlichen Ländern begrenzt bleiben. Die Verbreitung der kolorektalen ESD wird hierzulande wesentlich von den Trainingsmöglichkeiten und auch von technischen Vereinfachungen abhängen, die eine Reduktion des Zeitbedarfs ermöglichen.

KARGER
Fax +49 761 4 52 07 14
Information@Karger.com
www.karger.com

1662-6664/14/0301-0039$39.50/0

Accessible online at:
www.karger.com/vim

Prof. Dr. Franz Ludwig Dumoulin
Abteilung für Innere Medizin, Gemeinschaftskrankenhaus Bonn
Bonner Talweg 4–6, 53113 Bonn, Germany
f.dumoulin@gk-bonn.de

Introduction

Colorectal cancer incidence in Europe is high [1], and endoscopic screening for adenoma has been established with remarkable success [2]. Nevertheless, efficacy of screening endoscopy critically depends not only on a high adenoma detection rate but also on the completeness of endoscopic adenoma resection. Thus, occurrence of advanced adenoma is common after polypectomy [3], and it has been demonstrated that 27% of interval cancers developed at segments of previous polypectomy [4]. Moreover, incomplete polyp resection might account for up to 19% of interval cancers [5]. Even small-sized (10–20 mm) flat or serrated lesions are incompletely resected in up to one third of the cases [6]. In fact, endoscopic resection of sessile or flat lesions larger than 20 mm is usually not achieved en bloc, and recurrence rates of up to 31% have been reported after piecemeal (i.e. fragmented) endoscopic mucosal resection (EMR) [7]. Since histopathology cannot confirm completeness after piecemeal resection, short-term follow-up endoscopy within 2–6 months is the standard of care [8]. In contrast to EMR, endoscopic submucosal dissection (ESD) allows high en bloc resection and very low recurrence rates, even for larger flat or sessile colorectal lesions. Major disadvantages of ESD are high demands on technical skills, longer procedure times, and a higher perforation rate (the latter being probably of little clinical relevance since most perforations are treated during the ESD intervention). ESD has been developed and evaluated mainly in Asia, in particular in Japan; the experience with ESD is limited in the Western world.

Potential Indications for Colorectal ESD

En bloc resection by ESD is an attractive method for any large benign colorectal adenoma since histological confirmation of complete resection would eliminate the need for short-term endoscopic control after polypectomy. However, since ESD is technically demanding and needs long procedure times, more stringent criteria for colorectal ESD have been elaborated by the Japanese Colorectal ESD Standardization Implementation Working Group. These consensus recommendations include only larger-sized lesions (>20 mm) with suspected high-grade intraepithelial neoplasia or early cancer (laterally spreading tumor non-granular type, pseudodepressed or depressed lesions, irregular surface pattern suggestive of early submucosal invasion) or lesions with fibrosis including sporadic adenoma in chronic inflammation (e.g. ulcerative colitis) or residual carcinoma after previous endoscopic therapy [9, 10].

Practical Aspects of Colorectal ESD

ESD is performed with an endoscope equipped with an accessory water irrigation channel. Insufflation is done with carbon dioxide to reduce abdominal discomfort during long-lasting procedures [11]. Moreover, a transparent hood is attached to the tip of the scope to facilitate submucosal dissection. Also a careful characterization of the target lesion with high-definition or magnification endoscopy including chromoendoscopy is performed. Various classification systems are validated for the identification of malignancy and of deeper submucosal in-

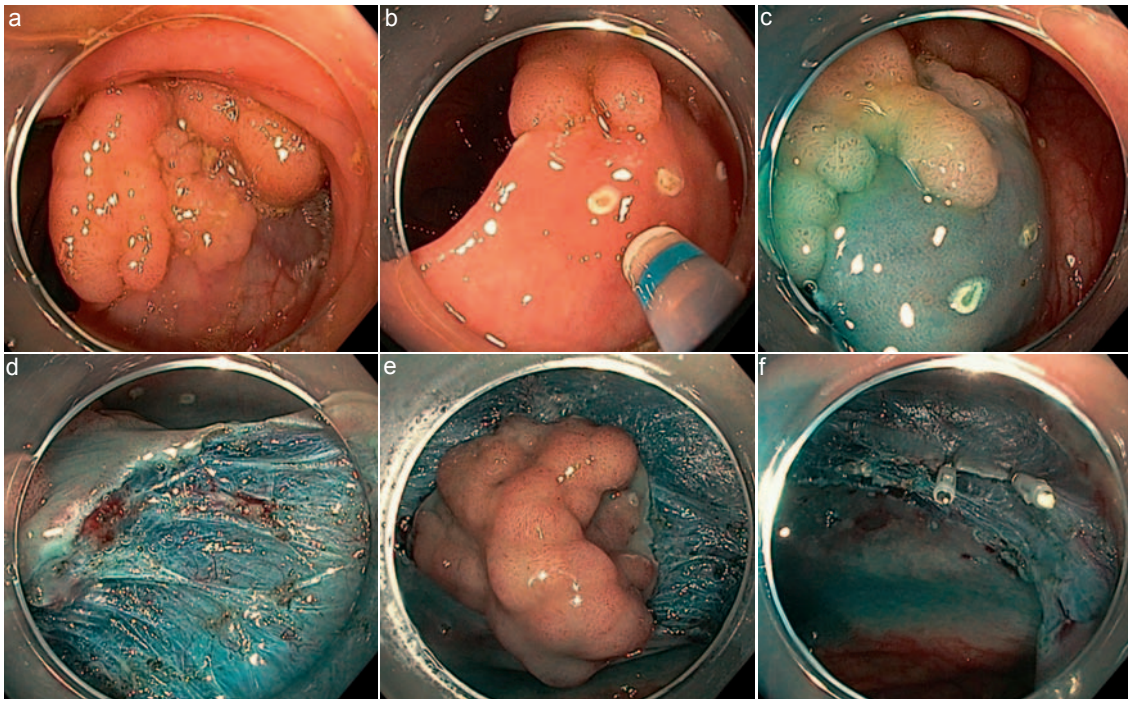

Fig. 1. Example of an ESD procedure: **a** A large sessile lesion (Paris classification 0–Is/0–IIa) was detected in the ascending colon. **b** Target lesion is surrounded by marking dots to facilitate resection. **c** Submucosal injection of 4% gelatine solution with a small amount of indigo carmine; injection is carried out with a small bore needle outside the lesion to avoid submucosal bleeding. **d** Opening of the submucosal space with traction on the specimen by gravity. **e** Subtotal preparation, and **f** resection area with hemoclips to prevent delayed bleeding.

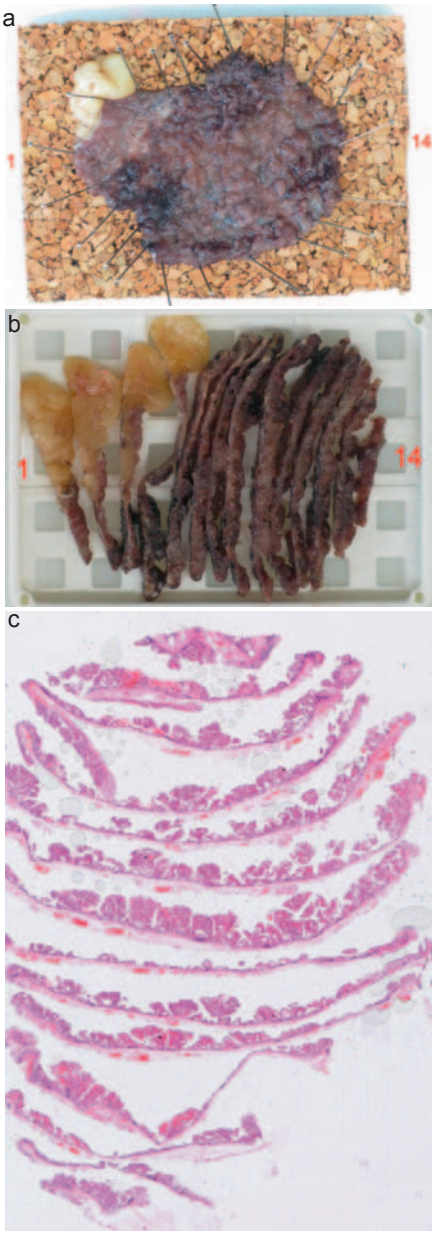

Fig. 2. Sample preparation and histopathological analysis. Special care is taken to correlate microscopic findings with endoscopy. Moreover, the margins of the specimen are meticulously inspected for residual adenoma/carcinoma. **a** ESD specimen pinned on corkboard to facilitate identification of margins. **b** Positioning of transverse sections. **c** Microscopic analysis allowing topographical correlation.

vasion (Paris classification [12], pit pattern classification [13], NICE classification [14]). In addition, endoscopic ultrasound is very useful for larger rectal lesions. After evaluation of the lesion, the borders are marked with coagulation current (figs. 1a, b). Next, submucosal injection is performed with a thin (25-G) injection needle (fig. 1c) using injection fluids that result in sustained elevation (e.g. glycerol, gelatin, or hyaluronic acid) and contain a small amount of dye (e.g. indigo carmine) for better visualization of the submucosal layer [10, 15–17]. A variety of knifes are available for mucosal incision/submucosal dissection (e.g. dual, hook, insulation-tipped (IT), triangle-tipped (TT) [18–21]), some of them allowing also for submucosal injection (e.g. flush knife [22] or hybrid knife [23, 24]). Hemostasis during the dissection procedure is achieved either with the knife itself in coagulation mode or – in the case of larger vessels – with dedicated hemostatic forceps or hemoclips. Submucosal dissection is then carried out paying attention to the patient's position to achieve traction on the specimen by gravity [25, 26] (figs. 1d, e). In difficult situations or locations, specific techniques or devices may be helpful to facilitate traction on the specimen [27, 28]. After the specimen is resected, hemostasis is secured by additional careful coagulation and/or hemoclips (fig. 1f). The specimen is then retrieved and stretched out (e.g. on a cork board) to facilitate further processing (fig. 2a). Cooperation with the pathologist is very important, and preparation of the ESD specimens should be performed to allow for correlation of the endoscopic/macroscopic appearance with histopathology. Particular care must be taken with the lateral and vertical margins in order to confirm complete resection of the lesion [29] (figs. 2b, c).

Clinical Studies on Colorectal ESD

Several large series on colorectal ESD have been published from Asian centers. However, most of the data are retrospective, and direct prospective comparative data on ESD versus EMR or surgery are not available. A recent systematic review reported resection rates of 90.5% (61–98.2%) for endoscopic en bloc resection and of 76.9% (58–95.6%) for histologically confirmed complete resection, with associated local recurrence rates of 1.9% (0–11%) [9]. In addition, there are several studies with >500 ESD procedures, including large single center series [25, 30], multicenter surveys [31, 32], and a prospective multicenter study [33]. These series confirm the high en bloc resection rates (up to 88.8% histologically confirmed complete resections) and the reported complication rates (perforation 4.8–5.4%, delayed perforation 0.4–0.7%, bleeding 1.5–1.7%). It was also demonstrated that ESD is feasible not only for the resection of adenoma or superficial cancers, but is also curative for submucosal invasive cancer. Thus, submucosal invasion limited to the upper 1,000 μm of the submucosal layer (sm1) is sufficiently treated with local resection if the tumor has a G1/G2 differentiation and no lymphatic or vascular invasion (L0, V0) [34–37].

When compared to EMR, data on ESD consistently show a higher en bloc resection rate/lower recurrence rate. Thus, in an analysis of 26 studies on EMR, en bloc resection for relatively smaller target lesions was possible in only 42.6% (19.2–91.8%) and recurrence rates were 17% (4.8–31.4%) for lesions resected in a piecemeal fashion [9]. In addition, several retrospective case series [38–41], a matched case control analysis [42], and a meta-analysis [43] were published on the comparative analysis of EMR versus ESD. All these reports show a higher efficacy of ESD for the resection of larger sessile or flat lesions, resulting in a lower recurrence rate. When analyzing risk factors for adenoma recurrence after EMR, associations were reported with size and morphology of the lesions

Table 1. Overview of European studies on colorectal ESD

Author, year [ref.]	Cases, n	Location (%)	Size, mm	Procedure time, min	En bloc rate, %	Perforation, %	Bleeding, %
Hurlstone et al., 2007 [57]	42	rectum (33.3)	31.0	n.a.	78.6	2.4	9.5
Farhat et al., 2011 [58], multicenter	85	rectum (84.7)	26.0	105	77.1	18.1	11.2
Probst et al., 2012 [59]	76	rectum (86.6)	45.5	176	81.6	1.3	7.9
Thorlacius et al., 2013 [61]	29	rectum (59.0)	26.0	142	72.0	6.9	3.3
Repici et al., 2013 [60]	40	rectum (100.0)	46.8	86.1	90.0	2.5	5.0
Sauer et al., 2013 [62]	83	rectum (18.0)	35.0	103	79.5	9.8	2.2

n.a. = Not applicable.

(higher risk of incomplete resection for serrated adenoma/flat adenoma), piecemeal resection, and number of fragments [6, 7, 44–46]. Data on complications after EMR/ESD show similar bleeding rates (EMR 0–11.1%; ESD 0.5–9.5%), but the perforation rate is higher for ESD (1.3–20%) than for EMR (0–5.8%). However, the vast majority of perforations occurring during ESD are small and easily treated during the procedure, and thus the actual need for emergency surgery does not differ for EMR versus ESD [31, 47–51]. ESD is technically demanding and does require long procedure times. Thus, a recent study comparing 1,029 cases of conventional EMR with 816 ESD procedures showed a significantly higher procedure time for ESD (96 min) than for EMR (18 min). Procedure times increased with the size of the lesion, although for very large lesions a comparison to laparoscopic surgery would be more appropriate [48, 49]. Comparative data are available for ESD versus surgery, but again without a formal head-to-head study. Two smaller retrospective studies found no significant difference for efficacy (including procedure time) and safety between ESD versus transanal endoscopic microsurgery (TEM) for the treatment of early rectal cancer [52, 53]. A recently published systematic review and meta-analysis of 11 ESD and 10 TEM studies showed higher en bloc resection rates and a reduced need for additional surgery for TEM, while recurrence rates were significantly lower after ESD and no difference in the overall complication rate was observed [54]. Finally, a comparative retrospective study from the National Cancer Center Tokyo found that ESD is equally effective as laparoscopic surgery for the treatment of early colorectal cancer, with significantly lower complication rates and shorter procedure times [55]. Indeed, the accompanying editorial called for an initiative to disseminate ESD for optimal treatment of early colorectal cancer [56]. While larger studies on colorectal ESD are almost exclusively from Asia, data on colorectal ESD from Western countries is mostly limited to the distal colon [57–62] (table 1).

Taken together, there are considerable advantages of ESD over EMR for the resection of larger sessile or flat lesions, in particular high en bloc resection rates and low recurrence rates. The major problem of ESD is the technical challenge and the relatively long procedure time. Compared with surgery, ESD shows similar performance as TEM for rectal lesions, while a clear advantage – both for clinical outcome and procedure time – was observed in a single comparative study for ESD versus laparoscopic surgery for the treatment of T1 colorectal carcinoma. Nevertheless, there still is a need for prospective comparative trials to better define the role of ESD in comparison to EMR or surgery.

Training for ESD

Since ESD requires advanced endoscopic skills, thorough training is mandatory for its safe use in patients. Algorithms for colorectal ESD training are available mainly from Japan [25, 63–65]. Emphasis is put on theoretical knowledge, diagnostic skills, and attendance of ESD procedures performed by experts. Later, hands-on training is started under the supervision of experts, starting with gastric ESD at easily accessible sites (i.e. antrum), and then continuing on to more complex procedures including rectal ESD and finally ESD in the proximal colon. It has been demonstrated that complication rates during the learning curve for gastric ESD do not differ between supervised trainees and experts [66]. The situation for an endoscopist willing to learn ESD is very different in the Western countries where experience with ESD is limited, the incidence of early gastric cancer is low, and starting ESD hands-on training with small early gastric cancer lesions under expert supervision is not a generally available option [67–69]. Therefore, it has been suggested to start with observation of ESD procedures performed by Asian experts, followed by hands-on training on isolated stomachs and finally life animal procedures including management of complications, before actually attempting colorectal ESD under expert supervision in patients [70]. It has also been suggested that colorectal ESD should be started on smaller-sized lesions in the rectum, gradually increasing the level of difficulty of the procedures (larger lesions, more proximal location) [70]. Indeed, this concept – both animal experimentation and tutorials with Japanese experts – has been successfully implemented under the auspices of the European Society of Gastrointestinal Endoscopy [71].

Optimizing the ESD Procedure: Current Developments

Modifications of the ESD technique are aiming at simplifying resection, reducing procedure time, and minimizing the risk of complications. Thus, submucosal gel/elastic polymer injection has been evaluated in animal models. These substances allowed long-lasting elevation and more efficient dissection [72–74] and even had autodissective properties [75], thus greatly reducing procedure time. Moreover, the hybrid knife [23, 24] or flush knife [22] allow submucosal injection and dissection to be carried out with a single device. Finally, specific cutting devices are being evaluated, e.g. a mucosectome with a short cutting blade [76] or a submucosal dissector [77].

Conclusion

ESD is an attractive endoscopic treatment modality for larger sessile or flat adenomas/superficial or slightly submucosal invasive colorectal cancers. The advantages of high en bloc resection rates/low recurrence rates are currently balanced by the high technical challenge of the method and the associated long procedure times. While colorectal ESD has recently become a standard procedure in major Asian endoscopy centers, propagation of ESD in Western countries will critically depend on opportunities for specialized training and probably also on technical developments to facilitate ESD and reduce procedure times.

Acknowledgement

FLD gratefully acknowledges Gerhard Kleber (Aalen, Germany) for initiating interest in colorectal ESD as well as Frieder Berr (Salzburg, Austria), Tsuneo Oyama, Akiko Takahashi (Nagano, Japan), Toshio Uraoka and Naohisa Yahagi (Tokyo, Japan) for theoretical instruction, tutorials, and hands-on training.

Disclosure Statement

The authors declare that there are no potential conflicts of interest relevant to the publication.

References

1 Ferlay J, Autier P, Boniol M, Heanue M, Colombet M, Boyle P: Estimates of the cancer incidence and mortality in Europe in 2006. Ann Oncol 2007;18: 581–592.
2 Pox CP, Altenhofen L, Brenner H, Theilmeier A, Von Stillfried D, Schmiegel W: Efficacy of a nationwide screening colonoscopy program for colorectal cancer. Gastroenterology 2012;142:1460–1467.e2.
3 Martinez ME, Baron JA, Lieberman DA, et al: A pooled analysis of advanced colorectal neoplasia diagnoses after colonoscopic polypectomy. Gastroenterology 2009;136:832–841.
4 Farrar WD, Sawhney MS, Nelson DB, Lederle FA, Bond JH: Colorectal cancers found after a complete colonoscopy. Clin Gastroenterol Hepatol 2006;4:1259–1264.
5 Robertson DJ, Lieberman DA, Winawer SJ, et al: Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut 2013;DOI: 10.1136/gutjnl-2012-303796.
6 Pohl H, Srivastava A, Bensen SP, et al: Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013;144:74–80.e1.
7 Woodward TA, Heckman MG, Cleveland P, De Melo S, Raimondo M, Wallace M: Predictors of complete endoscopic mucosal resection of flat and depressed gastrointestinal neoplasia of the colon. Am J Gastroenterol 2012;107:650–654.
8 Pox C, Aretz S, Bischoff SC, et al: S3-guideline colorectal cancer version 1.0 (article in German). Z Gastroenterol 2013;51:753–854.
9 Tanaka S, Terasaki M, Hayashi N, Oka S, Chayama K: Warning for unprincipled colorectal endoscopic submucosal dissection: accurate diagnosis and reasonable treatment strategy. Dig Endosc 2013;25:107–116.
10 Uraoka T, Saito Y, Yahagi N: What are the latest developments in colorectal endoscopic submucosal dissection? World J Gastrointest Endosc 2012;4: 296–300.
11 Saito Y, Uraoka T, Matsuda T, et al: A pilot study to assess the safety and efficacy of carbon dioxide insufflation during colorectal endoscopic submucosal dissection with the patient under conscious sedation. Gastrointest Endosc 2007;65:537–542.
12 No authors listed: The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003;58(suppl 6):S3–43.
13 Kudo S, Kashida H, Nakajima T, Tamura S, Nakajo K: Endoscopic diagnosis and treatment of early colorectal cancer. World J Surg 1997;21:694–701.
14 Hayashi N, Tanaka S, Hewett DG, et al: Endoscopic prediction of deep submucosal invasive carcinoma: validation of the narrow-band imaging international colorectal endoscopic (NICE) classification. Gastrointest Endosc 2013;78:625–632.
15 Fujishiro M, Yahagi N, Kashimura K, et al: Comparison of various submucosal injection solutions for maintaining mucosal elevation during endoscopic mucosal resection. Endoscopy 2004;36:579–583.
16 Fujishiro M, Yahagi N, Kashimura K, et al: Different mixtures of sodium hyaluronate and their ability to create submucosal fluid cushions for endoscopic mucosal resection. Endoscopy 2004;36:584–589.
17 Yamamoto H, Yahagi N, Oyama T, et al: Usefulness and safety of 0.4% sodium hyaluronate solution as a submucosal fluid 'cushion' in endoscopic resection for gastric neoplasms: a prospective multicenter trial. Gastrointest Endosc 2008;67:830–839.
18 Gotoda T, Kondo H, Ono H, Saito Y, Yamaguchi H, Saito D, et al: A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases. Gastrointest Endosc 1999;50:560–563.
19 Hotta K, Yamaguchi Y, Saito Y, Takao T, Ono H: Current opinions for endoscopic submucosal dissection for colorectal tumors from our experiences: indications, technical aspects and complications. Dig Endosc 2012;24(suppl 1):110–116.
20 Kodashima S, Fujishiro M, Yahagi N, Kakushima N, Omata M: Endoscopic submucosal dissection using flexknife. J Clin Gastroenterol 2006;40:378–384.
21 Oyama T, Tomori A, Hotta K, et al: Endoscopic submucosal dissection of early esophageal cancer. Clin Gastroenterol Hepatol 2005;3(suppl 1):S67–70.
22 Takeuchi Y, Shimokawa T, Ishihara R, et al: An electrosurgical endoknife with a water-jet function (flushknife) proves its merits in colorectal endoscopic submucosal dissection especially for the cases which should be removed en bloc. Gastroenterol Res Pract 2013;2013:530123.
23 Kahler GF, Sold MS, Post S, Fischer K, Enderle MD: Selective tissue elevation by pressure injection (STEP) facilitates endoscopic mucosal resection (EMR). Surg Technol Int 2007;16:107–112.
24 Belle S, Collet PH, Szyrach M, et al.: Selective tissue elevation by pressure for endoscopic mucosal resection of colorectal adenoma: first clinical trial. Surg Endosc 2012;26:343–349.
25 Yoshida N, Yagi N, Inada Y, Kugai M, Yanagisawa A, Naito Y: Prevention and management of complications of and training for colorectal endoscopic submucosal dissection. Gastroenterol Res Pract 2013;2013:287173.
26 Lee BI: Debates on colorectal endoscopic submucosal dissection – traction for effective dissection: gravity is enough. Clin Endosc 2013;46:467–471.
27 Oyama T: Counter traction makes endoscopic submucosal dissection easier. Clin Endosc 2012;45: 375–378.

28 Teoh AY, Chiu PW, Hon SF, Mak TW, Ng EK, Lau JY: Ex vivo comparative study using the Endolifter® as a traction device for enhancing submucosal visualization during endoscopic submucosal dissection. Surg Endosc 2013;27:1422–1427.
29 Nagata K, Shimizu M: Pathological evaluation of gastrointestinal endoscopic submucosal dissection materials based on Japanese guidelines. World J Gastrointest Endosc 2012;4:489–499.
30 Lee EJ, Lee JB, Lee SH, et al: Endoscopic submucosal dissection for colorectal tumors – 1,000 colorectal ESD cases: one specialized institute's experiences. Surg Endosc 2013;27:31–39.
31 Tanaka S, Terasaki M, Kanao H, Oka S, Chayama K: Current status and future perspectives of endoscopic submucosal dissection for colorectal tumors. Dig Endosc 2012;24(suppl 1):73–79.
32 Tanaka S, Tamegai Y, Tsuda S, Saito Y, Yahagi N, Yamano HO: Multicenter questionnaire survey on the current situation of colorectal endoscopic submucosal dissection in Japan. Dig Endosc 2010;22 (suppl 1):S2–8.
33 Saito Y, Uraoka T, Yamaguchi Y, et al: A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 2010;72:1217–1225.
34 Oka S, Tanaka S, Kanao H, et al: Mid-term prognosis after endoscopic resection for submucosal colorectal carcinoma: 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. Dig Endosc 2011;23:190–194.
35 Yamamoto S, Watanabe M, Hasegawa H, et al: The risk of lymph node metastasis in T1 colorectal carcinoma. Hepatogastroenterology 2004;51:998–1000.
36 Bosch SL, Teerenstra S, de Wilt JH, Cunningham C, Nagtegaal ID: Predicting lymph node metastasis in pT1 colorectal cancer: a systematic review of risk factors providing rationale for therapy decisions. Endoscopy 2013;45:827–834.
37 Carrara A, Mangiola D, Pertile R, et al: Analysis of risk factors for lymph nodal involvement in early stages of rectal cancer: when can local excision be considered an appropriate treatment? Systematic review and meta-analysis of the literature. Int J Surg Oncol 2012;2012:438450.
38 Lee EJ, Lee JB, Lee SH, Youk EG: Endoscopic treatment of large colorectal tumors: comparison of endoscopic mucosal resection, endoscopic mucosal resection-precutting, and endoscopic submucosal dissection. Surg Endosc 2012;26:2220–2230.
39 Terasaki M, Tanaka S, Oka S, et al: Clinical outcomes of endoscopic submucosal dissection and endoscopic mucosal resection for laterally spreading tumors larger than 20 mm. J Gastroenterol Hepatol 2012;27:734–740.
40 Tajika M, Niwa Y, Bhatia V, et al: Comparison of endoscopic submucosal dissection and endoscopic mucosal resection for large colorectal tumors. Eur J Gastroenterol Hepatol 2011;23:1042–1049.
41 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;24:343–352.
42 Kobayashi N, Yoshitake N, Hirahara Y, et al: Matched case-control study comparing endoscopic submucosal dissection and endoscopic mucosal resection for colorectal tumors. J Gastroenterol Hepatol 2012;27:728–733.
43 Cao Y, Liao C, Tan A, Gao Y, Mo Z, Gao F: Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. Endoscopy 2009;41:751–757.
44 Kim HH, Kim JH, Park SJ, Park MI, Moon W: Risk factors for incomplete resection and complications in endoscopic mucosal resection for lateral spreading tumors. Dig Endosc 2012;24:259–266.
45 Mannath J, Subramanian V, Singh R, Telakis E, Ragunath K: Polyp recurrence after endoscopic mucosal resection of sessile and flat colonic adenomas. Dig Dis Sci 2011;56:2389–2395.
46 Sakamoto T, Matsuda T, Otake Y, Nakajima T, Saito Y: Predictive factors of local recurrence after endoscopic piecemeal mucosal resection. J Gastroenterol 2012;47:635–640.
47 Niimi K, Fujishiro M, Kodashima S, et al: Long-term outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. Endoscopy 2010;42:723–729.
48 Ohata K, Nonaka K, Minato Y, et al: Endoscopic submucosal dissection for large colorectal tumor in a Japanese General Hospital. J Oncol 2013;2013: 218670.
49 Nakajima T, Saito Y, Tanaka S, et al: Current status of endoscopic resection strategy for large, early colorectal neoplasia in Japan. Surg Endosc 2013; 27:3262–3270.
50 Kim ES, Cho KB, Park KS, et al: Factors predictive of perforation during endoscopic submucosal dissection for the treatment of colorectal tumors. Endoscopy 2011;43:573–578.
51 Lee EJ, Lee JB, Choi YS, et al: Clinical risk factors for perforation during endoscopic submucosal dissection (ESD) for large-sized, nonpedunculated colorectal tumors. Surg Endosc 2012;26:1587–1594.
52 Kawaguti FS, Nahas CS, Marques CF, et al: Endoscopic submucosal dissection versus transanal endoscopic microsurgery for the treatment of early rectal cancer. Surg Endosc 2013;DOI: 10.1007/s00464-013-3302-z.
53 Park SU, Min YW, Shin JU, et al: Endoscopic submucosal dissection or transanal endoscopic microsurgery for nonpolypoid rectal high grade dysplasia and submucosa-invading rectal cancer. Endoscopy 2012;44:1031–1036.
54 Arezzo A, Passera R, Saito Y, et al: Systematic review and meta-analysis of endoscopic submucosal dissection versus transanal endoscopic microsurgery for large noninvasive rectal lesions. Surg Endosc 2013;DOI: 10.1007/s00464-013-3238-3.
55 Kiriyama S, Saito Y, Yamamoto S, et al: Comparison of endoscopic submucosal dissection with laparoscopic-assisted colorectal surgery for early-stage colorectal cancer: a retrospective analysis. Endoscopy 2012;44:1024–1030.
56 Swanstrom LL: Treatment of early colorectal cancers: too many choices? Endoscopy 2012;44:991–992.
57 Hurlstone DP, Atkinson R, Sanders DS, Thomson M, Cross SS, Brown S: Achieving R0 resection in the colorectum using endoscopic submucosal dissection. Br J Surg 2007;94:1536–1542.
58 Farhat S, Chaussade S, Ponchon T, et al: Endoscopic submucosal dissection in a European setting. A multi-institutional report of a technique in development. Endoscopy 2011;43:664–670.
59 Probst A, Golger D, Anthuber M, Markl B, Messmann H: Endoscopic submucosal dissection in large sessile lesions of the rectosigmoid: learning curve in a European center. Endoscopy 2012;44:660–667.
60 Repici A, Hassan C, Pagano N, et al: High efficacy of endoscopic submucosal dissection for rectal laterally spreading tumors larger than 3 cm. Gastrointest Endosc 2013;77:96–101.
61 Thorlacius H, Uedo N, Toth E: Implementation of endoscopic submucosal dissection for early colorectal neoplasms in Sweden. Gastroenterol Res Pract 2013;2013:758202.
62 Sauer M, Hildenbrand R, Bollmann R, Sido B, Dumoulin FL: Endoscopic submucosal dissection (ESD) of large sessile and flat neoplastic lesions in the colon: a single-center series with 83 procedures from Europe. Digestive Disease Week 2014, May 3–6, 2014. Chicago, IL, USA.
63 Niimi K, Fujishiro M, Goto O, Kodashima S, Koike K: Safety and efficacy of colorectal endoscopic submucosal dissection by the trainee endoscopists. Dig Endosc 2012;24(suppl 1):154–158.
64 Ohata K, Ito T, Chiba H, Tsuji Y, Matsuhashi N: Effective training system in colorectal endoscopic submucosal dissection. Dig Endosc 2012;24(suppl 1):84–89.
65 Sakamoto T, Saito Y, Fukunaga S, Nakajima T, Matsuda T: Learning curve associated with colorectal endoscopic submucosal dissection for endoscopists experienced in gastric endoscopic submucosal dissection. Dis Colon Rectum 2011;54:1307–1312.
66 Kakushima N, Fujishiro M, Kodashima S, Muraki Y, Tateishi A, Omata M: A learning curve for endoscopic submucosal dissection of gastric epithelial neoplasms. Endoscopy 2006;38:991–995.
67 Othman MO, Wallace MB: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) in 2011, a Western perspective. Clin Res Hepatol Gastroenterol 2011;35:288–294.
68 Draganov PV, Gotoda T, Chavalitdhamrong D, Wallace MB: Techniques of endoscopic submucosal dissection: application for the Western endoscopist? Gastrointest Endosc 2013;78:677–688.
69 Coman RM, Gotoda T, Draganov PV: Training in endoscopic submucosal dissection. World J Gastrointest Endosc 2013;5:369–378.
70 Uraoka T, Parra-Blanco A, Yahagi N: Colorectal endoscopic submucosal dissection: is it suitable in western countries? J Gastroenterol Hepatol 2013; 28:406–414.
71 Berr F, Ponchon T, Neureiter D, et al: Experimental endoscopic submucosal dissection training in a porcine model: learning experience of skilled Western endoscopists. Dig Endosc 2011;23:281–289.
72 Yu L, Xu W, Shen W, et al: Poly(lactic acid-co-glycolic acid)-poly(ethylene glycol)-poly(lactic acid-co-glycolic acid) thermogel as a novel submucosal cushion for endoscopic submucosal dissection. Acta Biomater 2013;pii:S1742-7061(13)00603-X.
73 Chandrasekhara V, Sigmon JC, Jr, Surti VC, Kochman ML: A novel gel provides durable submucosal cushion for endoscopic mucosal resection and endoscopic submucosal dissection. Surg Endosc 2013; 27:3039–3042.
74 Tran RT, Palmer M, Tang SJ, Abell TL, Yang J: Injectable drug-eluting elastomeric polymer: a novel submucosal injection material. Gastrointest Endosc 2012;75:1092–1097.
75 Khashab MA, Saxena P, Sharaiha RZ, et al: A novel submucosal gel permits simple and efficient gastric endoscopic submucosal dissection. Gastroenterology 2013;144:505–507.
76 Okamoto K, Kitamura S, Muguruma N, et al: Mucosectom2-short blade for safe and efficient endoscopic submucosal dissection of colorectal tumors. Endoscopy 2013;45:928–930.
77 Von Renteln D, Pohl H, Vassiliou MC, Rothstein RI: Colonic endoscopic submucosal dissection using a flexible Maryland dissector. Endoscopy 2009;41(suppl 2):E262–263.