Evaluation of the safety and feasibility of outpatient colorectal endoscopic submucosal dissection

Mike T. Wei, MD,[1] **Shai Friedland, MD**[1,2]

Stanford, Palo Alto, California, USA

Background and Aims: Endoscopic submucosal dissection (ESD) is increasingly used for resection of benign nonpedunculated colorectal polyps and early cancers. However, there is concern that adoption of ESD may be limited by increased resource utilization with routine postprocedure admission. As endoscopic closure of ESD wounds has improved, in 2022, we adopted an outpatient colorectal ESD protocol.

Methods: This study was a retrospective evaluation of adult patients who underwent colorectal ESD from January 2022 to April 2023. When technically feasible, the wound was closed by clips or suturing. After the procedure, patients were observed for up to 2 hours and discharged if they had no abdominal pain and no intraoperative muscle injury was present. We evaluated for operative success (en-bloc, R0, and curative resection) as well as safety (postprocedure pain, perforation, delayed bleeding).

Results: One hundred eleven lesions were removed by ESD in 105 consecutive patients. Nineteen lesions (17%) had prior EMR. All lesions were successfully removed: The en-bloc resection rate was 93% and the R0 and curative resection rate was 90%. Ninety-nine wounds (89%) were closed, most commonly using clips (60/111; 54%). Two small intraprocedural perforations occurred, both managed with clip closure, and the patients did not require admission. Among patients with defect closure, there were no delayed bleeds requiring hospitalization and only 1 episode of self-limited bleeding. In contrast, among 12 patients with resection sites not amenable to closure, there were 1 delayed bleed requiring hospitalization, 2 minor bleeds assessed at the emergency department, and 2 self-limited bleeds.

Conclusions: In this retrospective study, we demonstrated the feasibility of outpatient colorectal ESD. Among 105 patients, only 2 required hospital admission: 1 for postprocedure pain and 1 for delayed bleeding. We found that after endoscopic closure of ESD wounds, hospital admission was generally unnecessary and significant postprocedure bleeding was rare. (iGIE 2024;3:413-7.)

Endoscopic submucosal dissection (ESD) is increasingly used for resection of benign nonpedunculated colorectal polyps and early cancers. For lesions larger than 20 to 25 mm, ESD has been demonstrated to have higher R0 resection rates, lower recurrence rates, and improved histologic accuracy compared with EMR or other snare-based techniques.[1,2] However, there is concern about widespread adoption of ESD because of its potential for increased resource utilization in part because of protocols involving hospital admission after the procedure.

Traditionally, ESD patients have been admitted to the hospital for pain control and to monitor for delayed bleeding and perforation. More recently, several groups have reported ESD series with a significant fraction of patients treated as outpatients.[3,4] Because endoscopic closure of ESD wounds has improved with the addition of novel devices and techniques,[5,6] in 2022, we adopted an outpatient colorectal ESD protocol with hospital admission only for unplanned adverse events.

METHODS

One hundred five consecutive patients undergoing colorectal ESD from January 2022 to April 2023 were included in the analysis. Indications for ESD were nonpedunculated adenoma $\geq$20 mm, serrated lesion $\geq$20 mm with endoscopic appearance suggestive of dysplasia, nonpedunculated lesion with endoscopic appearance suggestive of early cancer, recurrent adenoma after prior endoscopic treatment, squamous dysplasia of the proximal anal canal, and rectal neuroendocrine tumor $\leq$10 mm. The institutional review boards at Stanford Hospital and Veterans Affairs Palo Alto Hospital approved the study. All patients had consented to the procedures.

Colonoscopy was performed by 1 endoscopist at Stanford Hospital (Palo Alto, Calif, USA) and Veterans Affairs Palo Alto Hospital (Palo Alto, Calif, USA). For patients who were on antiplatelet or anticoagulation medications, these were held in accordance to American Society for Gastrointestinal Endoscopy guidelines before the procedure.[7] Patients received sedation with monitored anesthesia care.

All colonoscopies were performed with a straight transparent hood (D-201; Olympus, Tokyo, Japan) attached to the end of the colonoscope. Polyps were categorized based on the Paris classification[8] and the Japan NBI Expert Team classification.[1,9] ESD was performed with an injecting needle-type knife (Proknife [Boston Scientific, Marlborough, Mass, USA] or GoldKnife [Micro-Tech Endoscopy, Ann Arbor, Mich, USA]) after an initial submucosal injection of hetastarch 6% with epinephrine (1:500,000) and indigo carmine (.004%). A continuous injection technique was used for dissection: When the knife was positioned at the submucosal cutting position, the assistant injected additional fluid in a slow continuous manner to provide additional elevation of the lesion. A partial mucosal incision was typically made on the distal side of the lesion followed immediately by submucosal dissection. The mucosal incision was gradually enlarged and then finished as submucosal dissection continued.

Hemostasis during the procedure was performed using the needle-type knife with coagulation settings. Incision and coagulation mode settings used were previously described by Fukami.[10] We used a VIO3 electrosurgical unit (Erbe, Tubingen, Germany). Mucosal incision and submucosal dissection were performed primarily with EndoCut I effect 2, and minor bleeding was treated using the knife tip with spray coagulation at 40 W. In cases in which use of the needle-type knife was not sufficient for hemostasis, a small coagulation forceps was used (Coagrasper hemostatic forceps; Olympus). When technically feasible, the wound was closed by available devices including clips with multiple grasping points (Lockado Clip; Micro-Tech Endoscopy), dual-action clips (DAT Closure Device; Micro-Tech Endoscopy), clips with sharp anchors (Mantis Clip; Boston Scientific), or endoscopic suturing devices (Overstitch and X-tack; Apollo Endosurgery, Austin, Tex, USA).

Trainees were involved in most procedures. Their level of participation depended on their level of experience, varying from performing the role of an equipment technician or nurse, mucosal incision, submucosal dissection, and mucosal closure. Trainees involved had prior experience with EMR or ESD in the colon, with a minimum of 50 prior EMR procedures and 2 years of general endoscopy experience. All procedures were performed with the endoscopist closely present throughout. Multiple closure techniques and devices were purposefully used to broaden the exposure of trainees to the wide variety of available accessories. Accurate time estimates for various portions of the procedures were not available because most of the procedure time was spent teaching trainees. Similarly, accurate estimates for closure time were not available because most of the time was spent teaching trainees closure technique.

Postoperative evaluation and disposition

After the procedure, patients were observed in the recovery area of the endoscopy unit for 1 to 2 hours and then discharged if they did not have abdominal pain or muscle injury and complete closure of the ESD site was performed. A full 2-hour observation was used when the wound was not closed. Patients with pain after the procedure were observed for up to 4 hours and then admitted for observation if the pain persisted.

All patients were contacted by telephone and/or e-mail 1 to 2 days after the procedure and again 10 to 14 days after the procedure. Hospital records and outside hospital records were also reviewed to ensure that all delayed adverse events were captured.

En-bloc resection was defined as complete resection of the lesion in 1 piece. R0 resection was defined as en-bloc resection of a neoplastic lesion (adenoma, serrated lesion, cancer, neuroendocrine tumor, or squamous dysplasia) with clear lateral and deep margins. Curative resection was defined as R0 resection without deep submucosal invasion ($\geq$500 μm), lymphovascular invasion, or poorly differentiated cancer.

Statistical analysis

In all analyses, $P < .05$ was considered significant. Excel (Microsoft Corp, Redmond, Wash, USA) was used to calculate the average, standard deviation, and frequency for patient and polyp characteristics. The χ^2 test was used to evaluate frequencies of categorical outcomes.

RESULTS

One hundred eleven lesions were removed by ESD in 105 consecutive patients. Patients had an average age of 65.5 years (standard deviation, 10.9) (Table 1). Most patients were men (64.8%), white (57.1%), and American Society of Anesthesiologists class II (61.0%). Most patients were not on antiplatelet (80.0%) or anticoagulation (91.4%) medications. Patients who were on antiplatelet or anticoagulation medications held their therapies in accordance with American Society for Gastrointestinal Endoscopy guidelines.[7] Patients on aspirin (18.1%) were permitted to maintain their aspirin therapy through the procedure.

Two patients had 2 separate lesions removed by ESD in a single procedure, and 2 patients had 3 separate lesions removed by ESD in a single procedure (Table 2). Seventy-three lesions (66%) were nonpolypoid. The mean lesion size was 28.2 mm. In terms of Paris classification, polyps were predominantly IIa (44.1%), Is/Isp (33.3%), and IIa+Is (14.4%). Of the 69 laterally spreading tumors, 59.4% were granular and 40.6% nongranular. Lesions were located in the cecum (9%), ileocecal valve (8%), ascending colon (21%), transverse colon (20%), descending colon (4%), sigmoid colon (20%), and rectum (19%). Eighty-five lesions (77%) had no prior treatment, whereas 19 (17%) had prior EMR with recurrence or incomplete treatment and 7 (6%) had prior submucosal

TABLE 1. Patient characteristics (n = 105)

Characteristics	Values
Age, y	65.5 ± 10.9
Sex	
Male	68 (64.8)
Female	37 (35.2)
Race/ethnicity	
White	60 (57.1)
Black	4 (3.8)
Hispanic	21 (20.0)
Asian	18 (17.1)
Unknown/not reported	2 (1.9)
American Society of Anesthesiologists class	
I	5 (4.8)
II	64 (61.0)
III	36 (34.3)
Periprocedural antiplatelet therapy	
None	84 (80.0)
Aspirin	17 (16.2)
Clopidogrel	2 (1.9)
Aspirin and clopidogrel	2 (1.9)
Periprocedural anticoagulation	
None	96 (91.4)
Apixaban	4 (3.8)
Rivaroxaban	5 (4.8)

Values are n (%) or mean ± standard deviation.

TABLE 2. Characteristics of lesions removed by endoscopic submucosal dissection (n = 111)*

Characteristics	Values
Polyp size, mm	28.2 ± 13.1
Paris classification	
Is/Isp	37 (33.3)
IIa	49 (44.1)
IIb	5 (4.5)
IIc	1 (.9)
IIa+IIc	3 (2.7)
IIa+Is	16 (14.4)
Japan NBI Expert Team classification	
1	3 (2.7)
2A	77 (69.4)
2B	31 (27.9)
Laterally spreading tumor	69 (62.2)
Granular	41 (59.4)
Nongranular	28 (40.6)
Location	
Cecum	10 (9.0)
Ileocecal valve	9 (8.1)
Ascending colon	23 (20.7)
Transverse colon	22 (19.8)
Descending colon	4 (3.6)
Sigmoid colon	22 (19.8)
Rectum	21 (18.9)
Pathology	
Adenoma†	83 (74.8)
High-grade dysplasia	14 (12.6)
Adenocarcinoma	9 (8.1)
Neuroendocrine tumor	1 (.9)
Other‡	4 (3.6)
No prior treatment	85 (76.6)
History of inflammatory bowel disease	7 (6.3)
En-bloc removal	103 (92.8)
Complete removal	111 (100)
R0	100 (90.1)
Curative resection	100 (90.1)

Values are n (%) or mean ± standard deviation.
*Two patients had 2 separate lesions removed by endoscopic submucosal dissection in a single procedure and 2 patients had 3 separate lesions removed by endoscopic submucosal dissection in a single procedure.
†Adenoma: 39 tubular adenomas, 28 tubulovillous adenomas, 8 sessile serrated adenomas, 5 traditional serrated adenomas, and 3 mixed traditional/sessile serrated adenomas.
‡No residual dysplasia or neuroendocrine tumor in 2 and inflammatory polyp in 2.

injection of a lifting agent but the planned endoscopy snare resection procedure was aborted by the physician performing the initial procedure and the patients were subsequently referred for ESD. Seven lesions (6%) were in patients with Crohn's colitis or ulcerative colitis.

All lesions were successfully removed. The en-bloc resection rate was 93%, the R0 resection rate was 90%, and the curative resection rate was 90%. Most lesions were adenomas (74.8%) followed by high-grade dysplasia (12.6%) and adenocarcinoma (8.1%). Of 111 lesions, 99 wounds (89%) were closed (Table 3), most commonly using clips with multiple grasping points (60/111; 54%). Of the 12 patients who did not have wound closure, 10 were because of a difficult location (involvement of ileocecal valve/ileal extension, rectal/anal lesion involving dentate line) and 2 were because of severe fibrosis, in which clips could not be deployed because they slipped off the edges. Two small (≤1 cm) intraprocedural perforations occurred, 1 in a patient with severe fibrosis from Crohn's disease and 1 in a patient with a malignant nonpolypoid lesion in the transverse colon with deep submucosal invasion. In both cases, the resection was completed after clip placement to treat the perforation. Both patients remained asymptomatic and did not require hospital admission and were given intraoperative antibiotics and were also discharged on a short course of antibiotics. The patient with deeply invasive cancer was recommended to have surgery. Of the patients evaluated, only 1 patient (.95%) required admission; this patient had postprocedure pain requiring overnight observation after resection of a 15-mm IIa+IIc Japan NBI Expert Team 2B adenoma in the sigmoid colon.

TABLE 3. Comparison of defect closure with no closure

	Closed (n = 99)	Not closed (n = 12)	*P* value
Complete removal	99 (100)	12 (100)	
R0	86/95* (91)	11/12 (100)	
Curative resection	86/95* (91)	11/12 (100)	
Closure technique			
Clips	89 (89.9)		
Overstitch	6 (6.1)		
X-Tack	4 (4.0)		
Adverse events			
Postprocedure pain, requiring admission	1 (1.0)	0 (0)	.727
Perforation, not requiring admission	2 (2.0)	0 (0)	.619
Perforation, requiring admission	0 (0)	0 (0)	
Delayed bleeding, overall	1 (1.0)	5 (41.7)	<.0001
Delayed bleeding with emergency department visit and/or admission	0 (0)	3 (25.0)	<.0001
Delayed bleeding requiring repeat endoscopy and/or surgery	0 (0)	0 (0)	

Values are n (%).
*Four patients were excluded where the endoscopic submucosal dissection showed no residual tumor or polyp (2 inflammatory bowel disease lesions with no dysplasia, 1 inflammatory polyp, and 1 neuroendocrine scar with no residual neuroendocrine tumor).

No muscle injury was observed, and the wound was closed with 8 clips. The patient's pain resolved overnight, and he was discharged home.

One patient experienced delayed bleeding that occurred 1 day after ESD of a 30-mm ileocecal valve adenoma. The wound was not closed because of significant extension into the terminal ileum. He was admitted to the hospital for 3 days; the bleeding resolved without treatment, and he did not require repeat colonoscopy or blood transfusion. Two additional patients presented to the emergency department for delayed bleeding; in both cases the bleeding appeared to be minor, and the patients did not require hospital admission or repeat endoscopy. Both patients had resection sites that were not amenable to closure. Another 3 patients reported self-limited bleeding at home within 10 days of the procedure, and no treatment was required. At the time of the resection procedure, the wound was closed in 1 of these patients but could not be closed in 2.

Follow-up colonoscopy was performed in 12 of 105 patients (11%). A 42-year-old woman with severe pulmonary and hepatic comorbidities who had a noncurative resection of a sigmoid colon cancer invading the deep submucosa experienced recurrence. She underwent surgical resection that demonstrated a T3N0 cancer.

DISCUSSION

In this series, we demonstrated the feasibility and safety of outpatient colorectal ESD. Among the 105 patients with 111 lesions removed by ESD, only 2 patients (2%) required hospital admission: 1 because of pain after the procedure and 1 because of delayed bleeding.

The main concerns regarding outpatient treatment are the possibility of delayed bleeding and of injury to the muscularis propria leading to delayed perforation.[11,12] Although delayed perforation is quite rare, with reported rates of approximately 1%, delayed bleeding is significantly more common, with a rate of 2% to 6%.[12,13] Wound closure after endoscopic resection has been demonstrated to reduce the risk of delayed bleeding[10] and in theory should also reduce or perhaps eliminate the risk of delayed perforation.

Although in the past it was difficult technically to close ESD wounds, with the arrival of multiple closure devices[5,14] and improved technique such as 2-layer clip-based suturing[6] or submucosal incision clipping,[15] most ESD wounds can now be closed effectively. Indeed, in our series, 99 of 111 wounds (89%) were successfully closed, and among these patients, there was no delayed bleeding requiring hospitalization and only 1 episode of self-limited bleeding that did not require evaluation in the emergency department. In contrast, among the 12 patients with resection sites that were not amenable to closure, 1 delayed bleeding event required hospitalization, 2 minor bleeding episodes were assessed on outpatient visits to the emergency department, and 2 self-limited bleeding events did not require evaluation in the emergency department. We therefore believe that after endoscopic closure of ESD wounds, hospital admission is generally not necessary and significant postprocedure bleeding is rare. Of note, use of the transparent cap at the tip of the colonoscope is helpful for endoscopic resection but does not interfere with resection closure. For some patients with wounds that are not amenable to closure, more data are needed to assess the safety of outpatient treatment. It is possible that newer gels and sprays that adhere to the resection site for several days and prevent bleeding may be

effective for these patients and facilitate outpatient treatment.[16]

We believe our results undermine one of the main arguments against the expansion of ESD for the treatment of most colorectal lesions ≥20 mm, namely the high cost of hospital admission in countries such as the United States. To this point, a retrospective study by Maselli et al[17] regarding outpatient ESD in Milan, Italy was able to generate savings of $1046.18 per patient compared with ESD with admission. Although the technical results of ESD are outstanding,[1,2] with high R0 rates of about 90% and recurrence rates often <1%, the safety, technical difficulty, time commitment, and need for hospitalization are commonly cited arguments for competing techniques such as piecemeal EMR, underwater EMR, and piecemeal cold snare resection. Although we did not specifically address the time needed for ESD in this article, because most procedures were partially performed by trainees at the 2 teaching hospitals, our results demonstrate that ESD can be performed safely and effectively in outpatients.

A weakness of our study is the absence of long-term follow-up, with only 12 of 105 patients (11%) undergoing follow-up colonoscopy. However, prior studies have demonstrated that high R0 and curative resection rates comparable with the 90% in our series portend extremely low recurrence rates of <2%.[1,2] The absence of any delayed perforations in our series is insufficient to draw conclusions about this rare event, which has a reported rate of approximately 1%. Larger studies are therefore needed to assess the efficacy of wound closure on delayed perforation.

In conclusion, our report suggests that outpatient colorectal ESD is a safe and effective option, particularly when routine wound closure is performed. We found that endoscopic closure of ESD wounds leads to a decreased risk of postprocedure bleeding and need for hospital admission.

DISCLOSURE

The following authors disclosed financial relationships: M. T. Wei: Consultant for Neptune Medical, Capsovision, and AgilTx. S. Friedland: Consultant for Intuitive Surgical and Capsovision.

Abbreviation: ESD, endoscopic submucosal dissection.

REFERENCES

1. Tanaka S, Kashida H, Saito Y, et al. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc 2020;32:219-39.
2. Jacques J, Schaefer M, Wallenhorst T, et al. Endoscopic en bloc versus piecemeal resection of large nonpedunculated colonic adenomas : a randomized comparative trial. Ann Intern Med 2024;177:29-38.
3. Tidehag V, Törnqvist B, Pekkari K, et al. Endoscopic submucosal dissection for removal of large colorectal neoplasias in an outpatient setting: a single-center series of 660 procedures in Sweden. Gastrointest Endosc 2022;96:101-7.
4. Baldaque-Silva F, Marques M, Andrade AP, et al. Endoscopic submucosal dissection of gastrointestinal lesions on an outpatient basis. United Eur Gastroenterol J 2019;7:326-34.
5. Wei M, Friedland S. Use of a novel dual-action clip for closure of complex endoscopic resection defects. VideoGIE 2022;7:389-91.
6. Masunaga T, Kato M, Sasaki M, et al. Modified double-layered suturing for a mucosal defect after colorectal endoscopic submucosal dissection (Origami method) (with video). Gastrointest Endosc 2023;97:962-9.
7. Acosta RD, Abraham NS, Chandrasekhara V, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc 2016;83:3-16.
8. Participants in the Paris Workshop. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003;58(6 Suppl):S3-43.
9. Inoue T, Nakagawa K, Yamasaki Y, et al. Underwater endoscopic mucosal resection versus endoscopic submucosal dissection for 20-30 mm colorectal polyps. J Gastroenterol Hepatol 2021;36:2549-57.
10. Fukami N. Endoscopic submucosal dissection: principles and practice. London: Springer; 2015.
11. Hirasawa K, Sato C, Makazu M, et al. Coagulation syndrome: delayed perforation after colorectal endoscopic treatments. World J Gastrointest Endosc 2015;7:1055-61.
12. Li R, Cai S, Sun D, et al. Risk factors for delayed bleeding after endoscopic submucosal dissection of colorectal tumors. Surg Endosc 2021;35:6583-90.
13. Kim ER, Chang DK. Management of complications of colorectal submucosal dissection. Clin Endosc 2019;52:114-9.
14. Wei MT, Friedland S. Use of anchor pronged clips to close complex polyp resection defects. VideoGIE 2023;8:245-6.
15. Otake Y, Saito Y, Sakamoto T, et al. New closure technique for large mucosal defects after endoscopic submucosal dissection of colorectal tumors (with video). Gastrointest Endosc 2012;75:663-7.
16. Hahn KY, Park JC, Lee YK, et al. Efficacy of hemostatic powder in preventing bleeding after gastric endoscopic submucosal dissection in high-risk patients. J Gastroenterol Hepatol 2018;33:656-63.
17. Maselli R, Galtieri PA, Di Leo M, et al. Cost analysis and outcome of endoscopic submucosal dissection for colorectal lesions in an outpatient setting. Dig Liver Dis 2019;51:391-6.

https://doi.org/10.1016/j.igie.2024.07.005

Received December 24, 2023. Accepted July 17, 2024.

Current affiliations: Department of Gastroenterology and Hepatology, Stanford University, Stanford, California, USA (1), Department of Gastroenterology and Hepatology, Veterans Affairs Palo Alto Health Care System, Palo Alto, California, USA (2).

Reprint requests: Mike T. Wei, MD, Department of Gastroenterology and Hepatology, Stanford University, 420 Broadway Street, Pavilion D, Redwood City, CA 94063.

How to cite iGIE articles: Johnson R, Webber C, Thompson TJ, et al. Article title. IGIE 2023;2:10-26.