Wide-field ESD for Barrett's adenocarcinoma at the gastroesophageal junction: technical approaches to facilitate en bloc R0 resection

Fabian Emura, MD, PhD, FASGE,^{1,2,3} Manuel Arrieta-Garcia, MD,^{1,3} Raúl Castillo-Delgado, MD,⁴ Huber Padilla-Zambrano, MD³

BACKGROUND

Endoscopic submucosal dissection (ESD) for Barrett's esophagus (BE) neoplasia is associated with high en bloc resection and an acceptable safety profile but with suboptimal curability rates (range, 56%-59%).¹ Two large Western studies showed that low R0 resection rates resulted from the high rate of positive lateral margins in ESD specimens (range, 82%-86%), which prompted either salvage ESD or additional surgical treatment.^{2,3} A U.S. multicenter ESD study found positive lateral margins in up to 70% of Barrett's adenocarcinoma (BA) at the gastroesophageal junction (GEJ) because of the increased technical complexity, poor maneuverability, and difficulty in evaluating the lesion's margin.⁴ Recently, ESD with wider resection margins (5-10 mm) has been proposed as an alternative to increasing the R0 resection rate and, therefore, the curability of Barrett's neoplasia.⁴ In a comparative study of wide-field (WF) ESD versus conventional ESD, WF-ESD resulted in a significantly higher curability rate, with fewer positive lateral margins and lower metachronous recurrences compared to conventional ESD.5 Technical approaches to reduce the positivity of lateral margins of ESD for BA located at the GEJ have not been described. We present a video case of WF-ESD for a BA of the GEJ and describe novel approaches for facilitating en bloc R0 resections (Video 1, available online at www. giejournal.org).

CASE

A 58-year-old male patient with a body mass index of 36 and a history of chronic GERD underwent an EGD. Whitelight high-definition examination revealed a COM3 BE and a 20-mm, IIa+IIc lesion located in the right quadrant of the GEJ at 40 cm from the incisors (Fig. 1A and B). In the direct view, the evaluation of the tumor was technically demanding, and the distal margin could not be evaluated. In the retroflexion view, the lesion's distal margin was clearly seen in contact with the proximal end of the gastric folds; indigo carmine chromoendoscopy revealed no ulcer, converging folds, or expanded change suggesting a superficial invasion. Nonmagnifying narrow-band imaging revealed a clear demarcation line with irregular vascular and mucosal patterns suggesting a T1a depth of invasion (Fig. 1C). Tumor biopsy revealed an intramucosal adenocarcinoma, and gastric biopsies showed nonatrophic chronic gastritis. The patient was scheduled for a WF-ESD aiming to eradicate the tumor and most of the surrounding non-neoplastic BE.

TECHNIQUE

The procedure was performed with the patient under intravenous sedation using an H-180J gastroscope and an EXERA II video processor (Olympus, Tokyo, Japan), an ERBE VIO 300D electrosurgical generator (ERBE Elektromedizin, Tubingen, Germany), a distal transparent cap (Olympus, Tokyo, Japan) and carbon dioxide insufflation. Esophageal and gastric marking dots were placed in direct and retroflex views, respectively, at least 5 mm from the lesion's margin using a conventional needle knife. A mixture of normal saline, indigo carmine dye, and epinephrine was used as the submucosal (SM) lifting solution. In direct view, a mucosal incision was made over the squamocolumnar esophageal epithelium at approximately 5 mm from the most proximal marking dot (Fig. 1D). Then, the entire procedure continued in the retroflex view and initiated with the circumferential incision using an IT-Knife2 (KD-611L, Olympus, Tokyo, Japan), maintaining a distance of at least 5 mm from all marking dots. The submucosal layer was dissected using endocut mode, effect 2, from the stomach to the esophagus and from the left and right lesion's sides toward the center of the lesion until en bloc resection was achieved (Fig. 1E and F). By this approach, the counter traction force of the gravity lifted the lesion allowing a clear visual of the dissection plane. Small vessels were selectively coagulated by mainly using the short blades located at the back of the IT-Knife2. The bleeding source from small vessels was identified by pouring a few drops of water over the pool of blood using the distal tip nozzle for lens cleaning and then was controlled using forced coagulation mode, effect 2. Although mild SM fibrosis was seen during the last part of the dissection,







Figure 1. Wide-field endoscopic submucosal dissection steps. **A**, In direct view, an elevated superficial lesion is observed at the gastroesophageal junction, but the distal margin cannot be evaluated. **B**, A 20-mm IIa+IIc lesion and the lesion's distal margin are seen in the retroflexion view using indigo carmine dye spraying. **C**, Nonmagnifying narrow-band imaging revealed a clear demarcation line and irregular vascular and structural patterns. **D**, The esophageal mucosal incision is made 5 mm from the most proximal marking dot. **E**, Submucosal dissection is performed using the IT-Knife2 in the retroflexion view. **F**, Hemicircumferential mucosal defect after endoscopic submucosal dissection.

an en bloc hemicircumferential resection was achieved without adverse events in 42 minutes. The size of the resected specimen was 48 mm, and the distance between the tumor edge and the whole radial specimen's margin was at least 10 mm (Fig. 2A and B). The WF-ESD steps accompanied by technical approaches and the endoscopic view are summarized in Table 1. The postoperative course was uneventful and the patient was discharged the same day with oral esomeprazole. Histopathology revealed a free lateral margin well-differentiated intranucosal adenocarcinoma without lymphovascular invasion and associated

intestinal metaplasia (IM) (Fig. 3A and B). Follow-up endoscopy showed a clean ESD scar, no stenosis, and 5-mm tongues of BE located at the left quadrant. Complete remission of IM was achieved after a single radiofrequency ablation (RFA) session using the HALO⁹⁰ RFA device.⁶

DISCUSSION

In contrast to the poor visualization, stability, and maneuverability inherent to ESD conducted using the



Figure 2. Evaluation of the resected specimen. **A**, The tumor and the specimen were 20 mm and 48 mm, respectively. **B**, The distance between the tumor edge and the whole radial specimen's margin was at least 10 mm.

TABLE 1. Wide-field endoscopic submucosal dissection steps and technical approaches		
Steps	Technical approach	Endoscopic view
Marking	\sim 5 mm from the tumor margin (needle knife)	Esophagus: direct view Stomach: retroflex view
Submucosal injection	Mixed solution of normal saline, epinephrine, indigo carmine dye, and hyaluronic acid (injection needle)	Esophagus: direct view Stomach: retroflex view
Esophageal mucosal pre-cut	Shallow incision after enough submucosal lifting (needle knife)	Direct view
Circumferential incision	\sim 5 mm from marking dots; include surrounding Barrett's esophagus and tongues (IT-Knife2)	Retroflexion view
Submucosal dissection	Fine lateral movements left to right and right to left from the stomach to the esophagus (IT-Knife2)	Retroflexion view
Hemostasia	Precise location of a bleeding site by pouring water throughout the dial tip lens cleaning nozzle. (IT-Knife2)	Retroflexion view

conventional direct view approach, the retroflexion view approach allowed the resection of a wide margin of gastric mucosa, facilitating an en bloc R0 resection in a relatively short time. This is noteworthy because the lesion was located at the right quadrant of the GEJ, and the patient was maintained in the left lateral position during the entire procedure. As a result, the counter-traction force of gravity pulled up the lesion allowing a better vision and minimizing the risk of perforation without the use of external traction methods. As reported by the authors here⁷ and other experts,^{8,9} when performing marking and mucosal cutting during some ESD procedures, a conventional needle knife is often the preferred tool over other dedicated ESD accessories. Advantages of using a needle knife include reusability, blade length adjustment, and low cost. Reports have addressed using the same ESD knife for SM dissection and minor bleeding control.^{10,11} In particular, the short blades of the IT-knife2 provide the ability to coagulate small blood vessels, control mild bleeding, and facilitate a faster dissection.9

This targeted approach to vessels eliminates the need for hemostatic forceps in all instances, reducing the operator's effort and the duration of the procedure. Although WF-ESD is a challenging procedure requiring training and expertise, it is a promising alternative to reduce the high rate of positive lateral margins when performing ESD for BA of the GEJ. Contrary to circumferential ESD for Barrett's neoplasia¹² and ESD cases encompassing \geq 75% of the esophageal circumference in which oral or local steroids are indicated to prevent stricture,^{5,13} prophylaxis using steroids was not indicated in the present hemicircumferential ESD case. To reduce the likelihood of recurrent dysplasia and metachronous cancer, current BE management strategies recommend endoscopic resection of visible neoplasia followed by RFA sessions until complete eradication of intestinal metaplasia is achieved.¹⁴ Further studies are warranted to demonstrate whether extensive removal of metaplastic tissue by using WF-ESD might increase the likelihood of achieving complete eradication of intestinal metaplasia with fewer RFA sessions.



Figure 3. Histopathological analysis. **A**, Panoramic hematoxylin and eosin staining revealed an intramucosal adenocarcinoma (*blue arrow*) without lymphovascular invasion. Normal esophageal squamous epithelium (*green arrow*) and low and high grade dysplastic glands in contact with the muscular mucosae (*yellow square*). **B**, High-power field. Goblet cells are seen confirming the presence of intestinal metaplasia (*yellow square*). Hyperchromatism, pseudostratification, nuclear atypia, and no lymphovascular invasion are observed (*blue square*).

DISCLOSURE

All authors disclosed no financial relationships. This work was supported in part by a grant in aid for the Comprehensive Strategy to Control Cancer in the Americas from the Emura Foundation for the Promotion of Cancer Research, ID No. 0223-17.

Abbreviations: BA, Barrett adenocarcinoma; BE, Barrett's esophagus; ESD, endoscopic submucosal dissection; GEJ, gastroesophageal junction; IM, intestinal metaplasia; RFA, radiofrequency ablation; SM, submucosal; WF, wide-field.

REFERENCES

- 1. Yang D, Zou F, Xiong S, et al. Endoscopic submucosal dissection for early Barrett's neoplasia: a meta-analysis. Gastrointest Endosc 2018;87:1383-93.
- **2.** Chevaux JB, Piessevaux H, Jouret-Mourin A, et al. Clinical outcome in patients treated with endoscopic submucosal dissection for superficial Barrett's neoplasia. Endoscopy 2015;47:103-12.
- Terheggen G, Horn EM, Vieth M, et al. A randomised trial of endoscopic submucosal dissection versus endoscopic mucosal resection for early Barrett's neoplasia. Gut 2017;66:783-93.
- 4. Yang D, Coman RM, Kahaleh M, et al. Endoscopic submucosal dissection for Barrett's early neoplasia: a multicenter study in the United States. Gastrointest Endosc 2017;86:600-7.
- Omae M, Hagström H, Ndegwa N, et al. Wide-field endoscopic submucosal dissection for the treatment of Barrett's esophagus neoplasia. Endosc Int Open 2021;9:E727-34.
- Barret M, Belghazi K, Weusten BL, et al. Single-session endoscopic resection and focal radiofrequency ablation for short-segment Barrett's esophagus with early neoplasia. Gastrointest Endosc 2016;84:29-36.
- Emura F, Mejía J, Donneys A, et al. Therapeutic outcomes of endoscopic submucosal dissection of differentiated early gastric cancer in a Western endoscopy setting (with video). Gastrointest Endosc 2015;82:804-11.

- Oda I, Gotoda T, Hamanaka H, et al. Endoscopic submucosal resection for early gastric cancer: technical feasibility, operation time and complications from a large consecutive series. Digest Endosc 2005;17:54-8.
- Ono H, Hasuike N, Inui T, et al. Usefulness of a novel electrosurgical knife, the insulation-tipped diathermic knife-2, for endoscopic submucosal dissection of early gastric cancer. Gastric Cancer 2008;11:47-52.
- Oyama T, Tomori A, Hotta K, et al. Hemostasis with hook knife during endoscopic submucosal dissection. Digestive Endoscopy 2006;18: S128-30.
- 11. Emura F, Calderon-Zapata D, Cano M, et al. Novel approaches to minimize intraoperative bleeding during endoscopic submucosal dissection of a large rectal lateral spreading tumor extended to the dentate line with internal hemorrhoids. VideoGIE 2021;6:344-6.
- 12. Emura F, Torres-Rincon R, Calderon-Zapata D, et al. Circumferential endoscopic submucosal dissection for the treatment of ultra-short-segment Barrett's adenocarcinoma with multifocal dysplasia. Video-GIE 2020;5:649-51.
- Lu Q, Wang J, Lv X, et al. Long-term outcomes of refractory esophageal strictures after endoscopic submucosal dissection of superficial esophageal neoplasms. BMC Gastroenterol 2022;22:147.
- 14. Emura F, Chandrasecar VT, Hassan C, et al. Rio de Janeiro Global Consensus on Landmarks, Definitions and Classifications in Barrett's Esophagus: World Endoscopy Organization Delphi Study. Gastroenterology 2022;163:84-96.e2.

Gastroenterology Division, Universidad de La Sabana, Chía, Colombia (1), Endoscopy, Clínica Imbanaco, Grupo Quironsalud, Cali, Colombia (2), Advanced GI Endoscopy, EmuraCenter LatinoAmerica, Bogotá DC, Colombia (3), Pathology, Clínica Imbanaco, Grupo Quironsalud, Cali, Colombia (4).

Copyright © 2022 American Society for Gastrointestinal Endoscopy. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

https://doi.org/10.1016/j.vgie.2022.08.004