Endoscopic mesorectal dissection for precise rectal cancer staging: trespassing the boundaries of lumenal rectal interventions CME

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BACKGROUND

Total mesorectal excision (TME) has been the primary treatment for patients with locally advanced rectal cancer (LARC). Still, it is associated with significant urinary, defecatory, and sexual dysfunction and a permanent stoma.[1] Surgical local excision in the form of transanal excision or transanal endoscopic microsurgery is widely performed for the treatment of T1 lesions[2] and, more recently, as adjuvant therapy for LARC.[3] Recent multicenter randomized controlled trials demonstrated that surgical local excision showed similar oncologic results to TME for T2-T3 cancer after neoadjuvant chemoradiotherapy.[4,5] No endoscopic alternatives can currently be offered for the multimodal treatment of LARC using standard equipment and conventional endoscopic submucosal dissection (ESD) devices. We describe a novel procedure, the endoscopic mesorectal dissection (EMD), for precise staging and as an organ-sparing alternative to surgical excision in the multimodal treatment of LARC.

CASE

A 79-year-old male patient presented with a 25-mm rectal polyp at a distance of 11 cm from the anal verge. High-definition white-light chromoendoscopy using indigo carmine dye disclosed a protruded and depressed lesion with irregular surface microvessels (Fig. 1A). Biopsy revealed a well-differentiated adenocarcinoma without lymphovascular invasion, and an EUS imaging disclosed invasion until but not going through the muscle layer without lymph node (LN) metastasis (Fig. 2). The estimated depth of invasion was T2, but the patient refused surgical treatment because of its associated adverse effects. The patient was scheduled for an EMD for precise tumor staging (Figs. 3 and 4).

PROCEDURE

The procedure was performed by an expert ESD endoscopist (F.E.) at the endoscopy suite under intravenous (IV) sedation using standard endoscopic equipment consisting of an H-180 gastroscope and an Elvis EXERA II video processor (Olympus, Tokyo, Japan), an ERBE VIO 300D electrosurgical generator (ERBE Elektromedizin, Tübingen, Germany), and carbon dioxide insufflation. Water instilled through the endoscope's working channel identified the lesion at the left lateral wall. A mixture of normal saline solution, indigo carmine dye, epinephrine, and hyaluronic acid (Mucoup, Tokyo, Japan) was used as the submucosal lifting solution. No lifting sign was observed (Fig. 1B). With the patient in the supine position, a mucosal, partial circumferential incision and submucosal dissection were performed at the proximal side in the retroflexion view using a Dual Knife (Olympus) and an ST Hood (Fujifilm, Tokyo, Japan) in Endocut mode effect 2. When severe fibrosis or submucosal tumor infiltration was encountered (Fig. 1C), the muscle layer was incised in a stepwise manner, the circular, external muscle layer first (Fig. 1D) and then, the longitudinal internal muscle layer until the mesorectal adipose tissue was exposed (Fig. 1E) using an IT nano (KD-612; Olympus) and an IT-2 (KD-611; Olympus). Then, the same approach was performed on the anal side until achieving an en bloc resection including underneath mesorectal adipose tissue. According to the studies of Hahnloser et al[6] and Bignell et al,[7] the mesorectum was left open (Fig. 1F). A Coagrasper (Olympus) in forced coagulation mode was used to control minor bleeding from the

Abbreviations: EMD, endoscopic mesorectal dissection; ESD, endoscopic submucosal dissection; FOLFOX, folinic acid-fluorouracil-oxaliplatin; IV, intravenous; LARC, locally advanced rectal cancer; LE, local excision; LN, lymph node; nCRT, neoadjuvant chemoradiotherapy; TAE, transanal excision; TEM, transanal endoscopic microsurgery; TME, total mesorectal excision.

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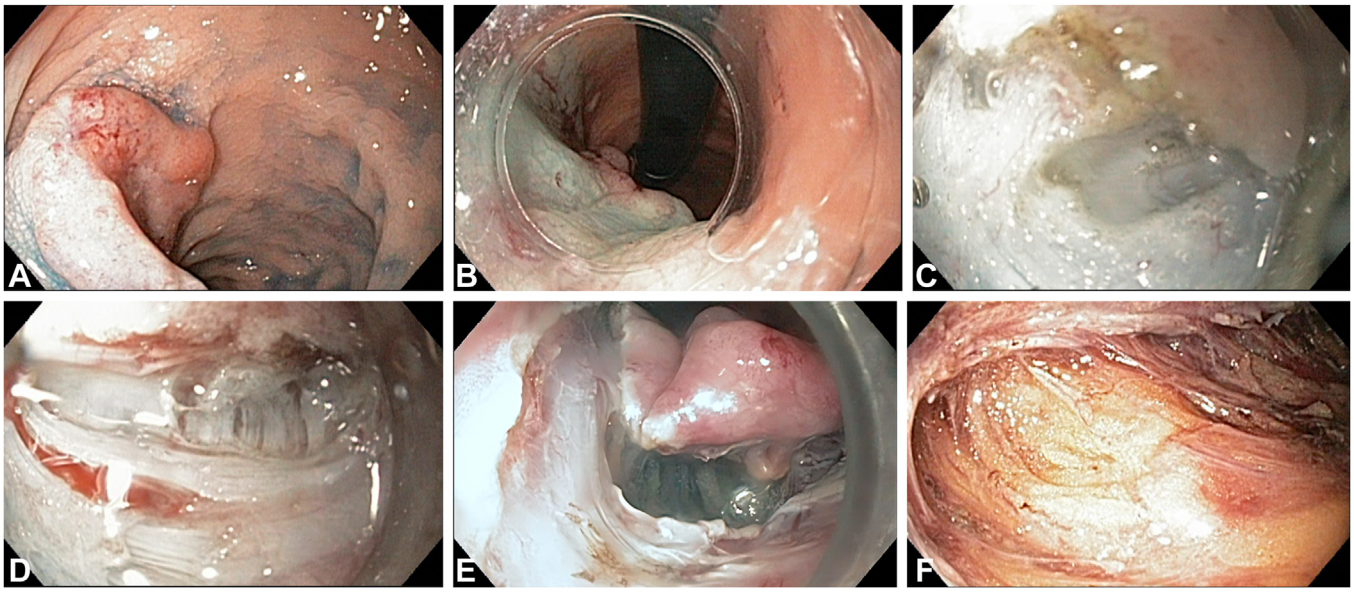

Figure 1. EMD steps. **A,** High-definition white-light chromoendoscopy disclosed a protruded and depressed rectal lesion with irregular surface microvessels. **B,** Submucosal injection showed a no-lifting sign. **C,** Fibrosis and tumor infiltration were seen in the submucosal layer. **D,** The circular muscle layer was dissected exposing the internal longitudinal muscle layer. **E,** Then, the longitudinal muscle layer was dissected exposing the mesorectal adipose tissue. The muscle layers with mesorectal adipose tissue were resected until en bloc dissection was achieved. **F,** Rectal wall defect post-EMD. *EMD*, Endoscopic mesorectal dissection.

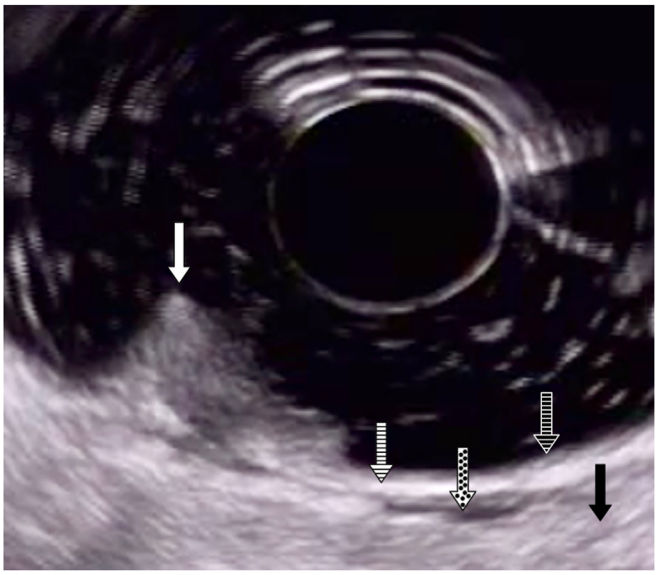

Figure 2. EUS image. EUS revealed a rectal tumor (*white arrow*), invading the submucosa (*narrow stripes arrow*) and muscularis propria (*dotted arrow*) but not going through it. Other rectal layers are the mucosa (*wide strips arrow*) and the mesorectum (*black arrow*).

mesorectum. The resected specimen's size was 30 mm (Video 1, available online at www.videogie.org).

OUTCOME

There were no intra- or postoperative adverse events. The patient was admitted for observation and maintained without

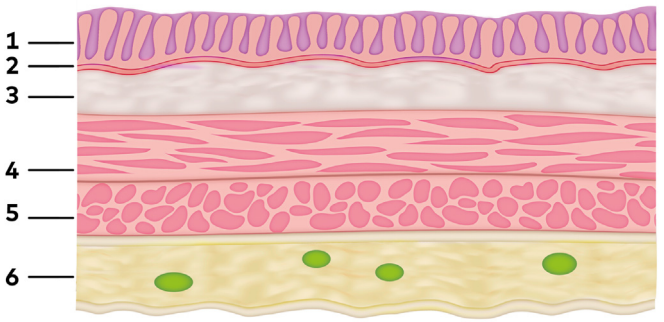

Figure 3. Illustration of a normal rectal wall. Mucosa (**1**), muscularis mucosae (**2**), submucosa (**3**), circular internal muscle (**4**), longitudinal external muscle (**5**), and mesorectal adipose tissue (**6**).

oral nourishment receiving IV administration of metronidazole and cefotaxime. Liquids were initiated at 24 hours and the patient was discharged home on the third postoperative day to complete a 2-week course of peroral antibiotics. Histopathology revealed a free-margin well-differentiated adenocarcinoma invading but not trans-passing the muscle layer without lymphovascular invasion. The mesorectal adipose tissue underneath was free of tumor (Fig. 5). A 2-week follow-up colonoscopy showed a healing scar without stenosis. The patient consented to undergo a TME due to the 11.7% risk of LN invasion for well-differentiated T2 tumors.[8] A colorectal anastomosis was carried out without postoperative adverse events. Histopathology revealed no residual tumor and 2 out of 37 positive LNs. After that, the patient received a chemotherapy regimen consisting of 6 FOLFOX (folinic

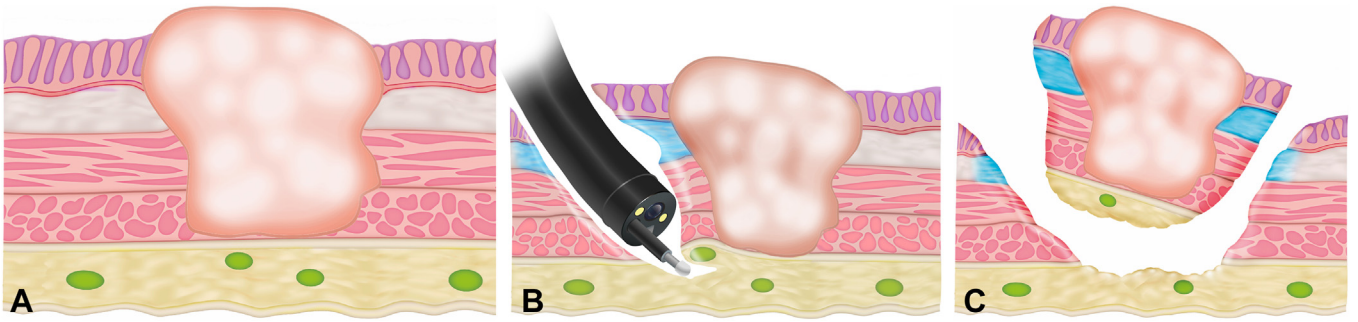

Figure 4. EMD technique. **A,** A LARC invading but not going through the muscle layer. **B,** During ESD, when tumor infiltration was found, the muscle layer was dissected stepwise: the circular layer first, followed by the longitudinal layer until the mesorectum was exposed. **C,** The rectal wall and the underlying mesorectum were removed en bloc for precise histologic assessment. *EMD*, Endoscopic mesorectal dissection; *LARC*, locally advanced rectal cancer.

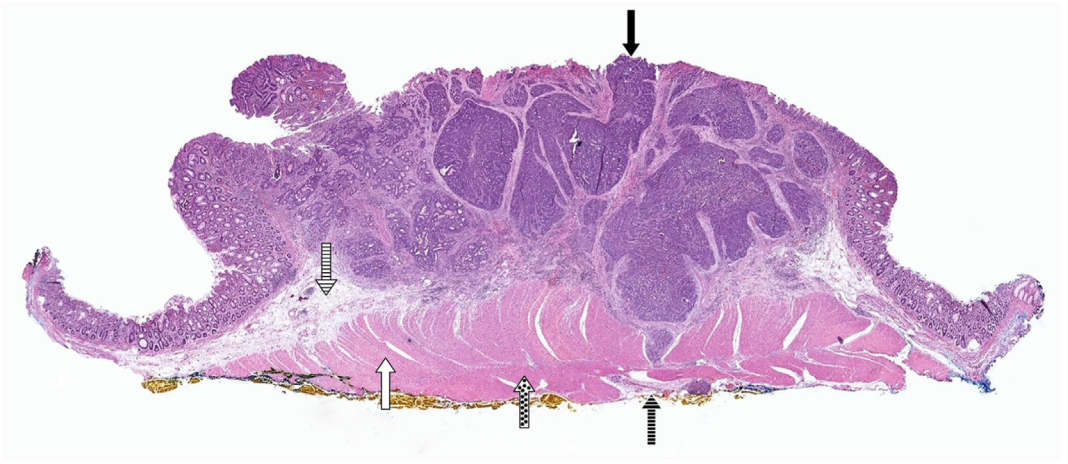

Figure 5. Histopathology. A panoramic 2× view using H&E staining revealed a rectal adenocarcinoma (*black arrow*) invading but not going through the muscularis propria. Rectal layers are identified as follows: submucosa (*narrow stripes arrow*), circular muscular (*white arrow*), longitudinal muscular (*dotted arrow*), and mesorectum (*wide stripes arrow*). H&E, orig. mag. ×100.

acid-fluorouracil-oxaliplatin) cycles and is currently disease-free. Although EMD may not influence the final treatment plan, it precisely assessed the tumor staging while preserving rectal integrity. The discrepancy between a negative EUS result before the EMD and the subsequent identification of 2 positive LNs following TME is unclear. This disparity may be attributable to the documented low accuracy (sensitivity 63% and specificity 80%) of EUS in assessing LNs in LARC.[9] On the other hand, although it can be speculated that the EMD affected LN positivity, a prior meta-analysis demonstrated that endoscopic resection does not affect LN cancer spreading in T1 colorectal cancer.[10] Further studies evaluating EMD and the risk of LN spreading in more advanced cancer stages are warranted. It is recommended that before considering an EMD procedure, cases should be strictly personalized through multidisciplinary discussions while taking into account the patient's preferences. Despite EMD seeming to trespass the current boundaries of luminal rectal endoscopic interventions, the dissection into the mesorectal tissue using the present ESD accessories was limited to a few millimeters. Although no perioperative adverse events were seen, larger studies are warranted to evaluate potential adverse events and dis-synergic wall effects and demonstrate the procedure's clinical effectiveness compared to standard methods. In brief, this work describes the EMD, a novel approach for precisely staging LARCs using standard equipment and conventional ESD devices. Based on recent rectal cancer guidelines,[11] EMD may play a role as an organ-preserving alternative before adjuvant therapy in patients with T1N0M0 to T2N0M0 cancer. On the other hand, in selected patients at stage T2-T3 after neoadjuvant chemoradiotherapy, EMD can be an alternative for salvage ESD[12] and surgical excision in patients who decline or are not suitable for transabdominal surgery.[4,5]

DISCLOSURE

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