Esophageal triamcinolone acetonide–filling method: a novel procedure to prevent stenosis after extensive esophageal endoscopic submucosal dissection (with videos)

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Background and Aims: Endoscopic submucosal dissection (ESD) for extensive esophageal carcinomas may cause severe stenosis requiring endoscopic balloon dilations (EBDs). A standard prevention method has not been established. We propose the esophageal triamcinolone acetonide (TA)–filling method as a novel local steroid administration procedure.

Methods: We enrolled 22 consecutive patients with early esophageal cancer who were treated using either subcircumferential or circumferential ESD (15 and 7 procedures, respectively) in this case series. Esophageal TA filling was performed on the day after ESD and 1 week later and was performed again if mild stenosis was found on follow-up. EBD with TA filling was performed only for severe stenosis that prevented endoscope passage. The primary endpoint was the incidence of severe stenosis. Secondary endpoints were the total number of EBDs and additional TA filling, dysphagia score, time to stenosis and to complete re-epithelialization, and any adverse events.

Results: The incidence of severe stenosis was 4.5% (1/22; confidence interval, .1%-22.8%), and EBD was performed 2 times in 1 patient. Mild stenosis was found in 9 patients. Additional TA filling was performed in 45.5% of patients (10/22; median, 5 times; range, 1-13). The dysphagia score deteriorated to 1 to 2 in 31.8% (7/22) but showed a final score of 0 after complete re-epithelialization in 90.9% (20/22). The median time to stenosis was 3 weeks (range, 3-4) and that to complete re-epithelialization was 7 weeks (range, 4-36). No severe adverse events occurred.

Conclusions: The esophageal TA-filling method is highly effective for preventing severe stenosis after extensive esophageal ESD. (Gastrointest Endosc 2018;87:380-9.)

The development of the endoscopic submucosal dissection (ESD) techniques has enabled endoscopic resection regardless of tumor size. However, extensive esophageal ESD is accompanied by severe stenosis in 66% to 75% of patients who undergo subcircumferential resection that involves over three-fourths of the esophageal circumference and in 100% of patients with circumferential resection if no preventive procedures are used.[1-4] For relieving severe esophageal stenosis, frequent endoscopic balloon dilation (EBD) is required,

Abbreviations: EBD, endoscopic balloon dilation; ESD, endoscopic submucosal dissection; TA, triamcinolone acetonide.

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This video can be viewed directly from the GIE website or by using the QR code and your mobile device. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.

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leading to a medical economic load, a decrease in patients' quality of life, and a risk of adverse events such as esophageal perforation.[5-7]

Some preventive measures for esophageal stenosis after extensive ESD have been reported, including preventive EBD, esophageal local steroid injection, oral steroids, temporary insertion of a self-expandable metallic stent, patching with a polyglycolic acid sheet, and transplantation of an oral mucosal epithelial cell sheet. Preventive EBD shows a certain degree of preventive effect but requires frequent procedures—30 or more—especially after circumferential ESD.[5,6] Two administration methods have been reported as effective and feasible for steroid use: esophageal local injection of triamcinolone acetonide (TA) and oral prednisolone.[2,3,5,8] Local TA injection, probably the most widely adopted preventive method, is reportedly performed once or several times, either immediately after or several days after ESD. The incidence of severe stenosis is reportedly suppressed to 10% to 19% for the patients who underwent subcircumferential ESD.[2,3] However, it is often technically difficult to inject TA evenly into the submucosal layer of an extensively resected site without drug leakage,[9] and intramuscular injection has the risk of delayed perforation or esophageal abscess.[10,11] Oral prednisolone administration may be the most inexpensive and technically easy of all the stenosis-prevention procedures. However, the reported dosage regimen starts at 30 mg/day and gradually tapers over 8 weeks, conferring a risk of adverse events with this long-term steroid use.

Two types of expandable metallic stents are available for temporary placement: a covered type and a biodegradable type. Both types are reportedly initially effective, but more than half of patients experience esophageal restenosis after stent removal or fragmentation.[12,13] Finally, as covering materials for the resected surface, 2 types of pasting products have been reported: the polyglycolic acid sheet is an absorbable mesh used to seal the tissue defect with fibrin glue during surgery, and the oral mucosal epithelial sheet is fabricated ex vivo by culturing isolated epithelial cells taken from the oral mucosa.[14-16] Both methods reportedly decrease the esophageal stenotic ratio after extensive ESD but require a skilled technician and a long procedure time to patch over a large area of resected surface. Moreover, fabricating the oral epithelial cell sheet is costly and technically possible only at certain institutions. Thus, the prophylactic treatment for the stenosis is very important after extensive esophageal ESD, but previously reported measures still have the problems of feasibility and safety.

As a novel procedure for the local administration of steroids, which may solve the problems concerning the esophageal local TA injection, we propose the esophageal TA-filling method. This method fills the esophagus with a saline solution of TA for a certain time, in expectation of even drug infiltration into the extensive resected surface. We anticipate a high preventive effect for esophageal stenosis after extensive ESD and expect this will be a simple and feasible procedure. In this case series we have analyzed the clinical efficacy and safety of the esophageal TA-filling method for the patients who underwent esophageal extensive ESD.

METHODS

Participants

Between December 2014 and September 2016, 22 consecutive patients were enrolled. All patients were treated for early-stage esophageal cancer with either subcircumferential (at least three-fourths but not the entire circumference) or circumferential ESD followed by esophageal TA filling at the Tottori Municipal Hospital and Shimane University Hospital. All participants were preoperatively diagnosed with superficial esophageal squamous cell carcinoma without lymph node or distant metastasis by endoscopic examination and CT.

The study protocol was approved by the medical ethics committee of the institutions, and written informed consent was obtained from all participants. The present study is a retrospective, single-arm analysis, but the enrolled participants represent an unselected consecutive population and faithfully followed the study protocol.

Esophageal TA-filling method

The esophageal TA-filling procedure was performed twice: on the day after ESD (postoperative day 1) and 1 week later (postoperative day 7) to enhance the therapeutic effect. Most patients were administered with scopolamine butylbromide (10 mg) or glucagon (.5 mg) to inhibit their esophagogastric peristalsis before the procedure.

First, an endoscope was inserted to the gastric antrum and pulled back to the esophagus, at the oral side of the resected site, suctioning as much esophagogastric air as possible. The endoscopic air supply system was shut off to avoid inadvertent airflow. Second, a saline solution containing 80 mg TA in 4 mL was slowly infused directly from the forceps channel and followed by an additional 20 mL of pure saline solution infusion to push out the drug solution and fill in the esophagus. Sufficient esophagogastric deaeration in the left lateral decubitus position inhibited outflow of the drug solution because of gravity (with subsequent replacement by intragastric air). For 2 minutes after drug infusion, any remaining intraesophageal air was endoscopically suctioned to allow sufficient contact of the drug solution with the resected surface.

These endoscopic procedures were performed with the patient under conscious sedation to avoid the gag reflex, which could cause the patient to vomit up the drug solution. The midazolam (2-5 mg) and pentazocine (7.5-15 mg) were intravenously administered, monitoring blood pressure, respiration rate, and blood oxygen concentration. When