Natural history and management of refractory benign esophageal strictures CME

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Background and Aims: The natural history of refractory benign esophageal strictures (RBES) is unclear, and surgery or percutaneous endoscopic gastrostomy (PEG) may be the only viable long-term options. The aim of the present study was to assess the long-term outcomes of patients with RBES.

Methods: Clinical data of consecutive patients with RBES treated in the previous 15 years in 2 tertiary-care referral academic centers with specialized interest in esophageal stricture management were retrospectively analyzed. RBES was defined as the persistence and/or recurrence of dysphagia despite at least 5 dilation sessions and/or cycles with dilation to at least 14 mm. Information regarding the use of dilation or stents and the dysphagia-free period between subsequent interventions and adverse events was collected. Clinical success was defined as no need for endoscopic interventions for at least 6 months; unfavorable outcomes were defined as the need for endoscopic treatment at the end of follow-up, surgery, or percutaneous endoscopic gastrostomy (PEG). Predictors of unfavorable outcomes were assessed by multivariate analysis. A linear mixed-effect model was used to measure dysphagia-free period changes over time.

Results: Overall, 70 patients with RBES (46 male; mean age 60 years) were followed for a mean of 43.9 months (range 3.7-157 months). Caustic, postradiotherapy, surgical, mixed, and postinflammatory etiology accounted for 10%, 14.3%, 31.4%, 40%, and 4.3% of causes, respectively. All patients underwent sequential sessions of pneumatic or bougie dilation, with a median of 15.5 dilation sessions per patient. Self-expandable metal stents (SEMSs) and biodegradable stents were placed in 18 (25.7%) and 14 (20%) patients, respectively. RBES resolution was achieved in only 22 of 70 (31.4%) patients. Two deaths (3%) were related to RBES. The success rate was lower in those who also were treated with endoprosthetics (odds ratio [OR] 3.7; 95% confidence interval [CI], 1.01-18.0). The mean dysphagia-free period was 3.3 months (95% CI, 2.4-4.1) for patients treated with dilation and 2.4 months (95% CI, 1.2-3.6) for those treated with stents ($P = .062$). Over time, the total dysphagia-free period increased at a rate of 4.1 days (95% CI, 1.7-6.4) per dilation. There was no difference in the rate of change across groups defined by sex ($P = .976$), age ($P = .633$), or endoscopic treatment ($P = .267$).

Conclusions: Our multicenter series showed a disappointing long-term outcome for RBES, with only 1 of 3 achieving clinical resolution. The dysphagia-free period was relatively short, affecting the quality of life. Endoprosthetics did not appear to affect the natural history of RBES. (Gastrointest Endosc 2016;84:222-8.)

Benign esophageal strictures have multiple etiologies, including caustic ingestion, peptic disease, esophageal surgery, and radiotherapy.[1,2] These strictures have a negative impact on the quality of life, mainly because of dysphagia, and they may result in severe adverse events, such as malnutrition, weight loss, and aspiration.[3] Endoscopic

Abbreviations: PEG, percutaneous endoscopic gastrostomy; SEMS, self-expandable metal stent; SEPS, self-expandable plastic stent; RBES, refractory benign esophageal stricture.

DISCLOSURE: *All authors disclosed no financial relationships relevant to this publication.*

See CME section; p. 329.

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2016.01.053

Received October 14, 2015. Accepted January 23, 2016.

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dilation with bougies or balloons is the standard treatment for such strictures.[4] However, 30% to 40% will recur during long-term follow-up, requiring repeated dilation or surgery.[1,5,6] When the persistence or recurrence of dysphagia occurs despite at least 5 dilation sessions with dilation to at least 14 mm, the condition may be defined as a refractory benign esophageal stricture (RBES).[5]

In order to avoid surgery or lifelong percutaneous endoscopic gastrostomy (PEG) placement, various therapeutic options for RBES have been proposed. Injection of steroids has been proposed to increase the efficacy of the dilation procedure. More recently, self-expandable plastic or metal stents (SEPSs/SEMSs) have been proposed in patients with RBES[2,7-21] as well as self-dilation at home.[22] However, the efficacy of these interventions remains uncertain because of the mixed outcomes of the studies and the short-term clinical follow-up.[3,4,6,23] The aim of our study was to assess the long-term (≥6 months) outcomes of patients with RBES.

PATIENTS AND METHODS

Patients and data collection

Clinical charts of patients who were managed over the previous 15 years in 2 tertiary-care referral academic centers (Humanitas Research Hospital, Milan, Italy, and Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA) were retrospectively reviewed, and patients who had a diagnosis of refractory or recurrent esophageal strictures, defined as the persistence or recurrence of dysphagia despite at least 5 endoscopic treatment sessions, were selected. Data were retrieved from electronic databases for the period covered by the study in both centers. The patients were treated from November 1999 to October 2012 and were followed until August 2014. The demographic and clinical data of each patient, including sex, age at diagnosis, stricture etiology, stricture site and length, type and number of treatments applied, dysphagia-free intervals between treatments, final outcomes, and adverse events were extracted from the electronic medical records. Patients were excluded if they were aged <18 years, had received <5 endoscopic treatments at each of the 2 tertiary-care centers, or presented with active inflammation or malignant dysphagia. The baseline date for analysis was considered to be the date of the first endoscopic procedure. The study protocol was approved by the institutional review board at both institutions. Written informed consent for each procedure was routinely obtained from each patient. There was no external funding for this study.

Endoscopic management and follow-up

Patients were treated following local clinical practice in each institution in accordance with best practices. Various types of gastroscopes (standard or high definition, with 5.4-11.6 mm diameters; Olympus [Tokyo, Japan], Fujinon [Omiya, Japan], and Pentax [Hoya Corporation, Japan]), with or without radiologic assistance, were used according to local availability, stricture characteristics, and type of treatment applied. Treatments included dilation—both bougie and balloon-assisted—steroid injection, placement of endoprosthetics (including SEPSs, SEMSs, and biodegradable stents), PEG placement, and surgery. Dilation was the standard of care for all patients, with other alternatives, such as fully covered SEMSs and biodegradable stents placed on a case-by-case basis at the discretion of the endoscopist performing the procedure (A.R., M.K.), after an appropriate discussion with surgeons, internists, a dietician, and oncologists as needed. Type of stents and timing of placement varied over time based on local availability of specific types of stents. Indication for stent placement was not uniform and was influenced by a number of factors including early dysphagia recurrence, stricture morphology and location, and proximity of the patients to the hospitals. Because of the off-label use of some of these stents (biodegradable stents are approved for benign indications in Europe), a specific informed consent was signed by the patients in case of stent placement. Fully covered SEMSs were removed after 12 weeks according to protocol in both centers. Each endoscopic procedure was performed according to protocols described in detail elsewhere.[3,6,19,20]

Most patients had only 1 treatment modality per dilation session. Usually patients were given an appointment for further endoscopic treatment based on their clinical histories (generally 3-6 weeks later) or were treated on an as-needed basis at dysphagia recurrence. Some patients would undergo intensive courses of high-frequency serial dilations and/or stent placement at short intervals, every 2 to 3 days. For the purpose of this article, we considered all the short-interval treatments performed within 7 days as part of the same cycle of treatment because the time interval between each single dilation in such cases could not be considered as a dysphagia-free period.

Outcomes

The primary outcome was the clinical resolution of dysphagia. This was defined as the maintenance of dysphagia-free status for at least 6 months with no need for further intervention at the end of follow-up, whereas an unfavorable outcome was defined as a need for further endoscopic treatment, surgery, or PEG. Secondary outcomes included the dysphagia-free intervals (both as an overall result as well as in the subgroups of patients receiving dilation or stent therapy), safety (serious adverse events and death), percentage of patients requiring surgery, and their long-term results. The dysphagia-free interval was calculated as the time between 2 successive treatments. Serious adverse events were defined as any adverse event that required or extended the patient's hospital stay, required additional endoscopic or surgical treatment, or that caused death.