Early metal stent insertion fails to prevent stricturing after single-stage complete Barrett's excision for high-grade dysplasia and early cancer CME

Bronte A. Holt, MBBS, BMedSc, FRACP,[1,2] Vanoo Jayasekeran, MBBS, FRACP, PhD,[1] Stephen J. Williams, MBBS, FRACP, MD,[1] Eric Y.T. Lee, MBBS, FRACP,[1] Farzan F. Bahin, MPhil, MBBS,[1] Rebecca Sonson, BN,[1] Reginald V. Lord, MBBS, MD, FRACS,[3] Michael J. Bourke, MBBS, FRACP[1,2]

Sydney, New South Wales, Australia

Background: Barrett's esophagus with high-grade dysplasia (HGD) or intramucosal adenocarcinoma (IMC) can be effectively treated by single-session EMR, resulting in complete Barrett's excision (CBE). CBE provides accurate histology for staging and clinical confirmation of neoplasia eradication but is limited by a high risk of esophageal stricture formation.

Objective: To evaluate the effectiveness of prophylactic temporary esophageal stenting to prevent post-CBE stricture formation.

Design and Setting: Single-center, investigator-initiated feasibility study.

Patients: Circumferential, short-segment Barrett's esophagus ($\leq$C3$\leq$M5) with HGD or IMC.

Intervention: Single-stage CBE and insertion of a fully covered metal esophageal stent at 10 days that was removed at 8 weeks. Patients were followed for a minimum of 2 surveillance endoscopies.

Main Outcome Measurement: Symptomatic esophageal stricture formation.

Results: At the end of the follow-up period, 8 patients (57.1%) required esophageal dilation for symptomatic CBE-related (n = 7) or stent-related (n = 4) strictures. A median of 3 surveillance endoscopies were performed over a median endoscopic follow-up of 17 months (range 4-25 months). Single-stage CBE successfully eliminated Barrett's intestinal metaplasia and neoplasia in 71.4% and 92.9% of patients, respectively. Four patients were admitted to the hospital, and 4 patients had early stent removal because of pain or dysphagia.

Limitations: Single-center feasibility study.

Conclusions: In a prospective study evaluating prophylactic esophageal stent insertion after single-stage CBE, esophageal strictures formed in more than of half the study cohort, and stents were associated with significant morbidity. An alternative method to reduce stricture formation is required. (Clinical trial registration number: NCT01554280.) (Gastrointest Endosc 2015;81:857-64.)

Abbreviations: BEF, bronchoesophageal fistula; CBE, complete Barrett's excision; CR-IM, complete response–intestinal metaplasia; CR-N, complete response–neoplasia; DS, dysphagia score; HGD, high-grade dysplasia; IM, intestinal metaplasia; IMC, intramucosal adenocarcinoma; LGD, low-grade dysplasia; RFA, radiofrequency ablation.

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Current affiliations: Department of Gastroenterology and Hepatology, Westmead Hospital (1), Sydney Medical School, University of Sydney (2),

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The increasing incidence of Barrett's esophagus is significant because of the associated risk of esophageal adenocarcinoma.[1-7] Barrett's mucosa undergoes a stepwise neoplastic progression, from intestinal metaplasia (IM) with no dysplasia through low-grade dysplasia (LGD) and high-grade dysplasia (HGD) stages to invasive adenocarcinoma.[8] Although the overall risk of esophageal adenocarcinoma in Barrett's esophagus is low,[9,10] the diagnosis of HGD and intramucosal adenocarcinoma (IMC) requires prompt intervention because of the risk of progression to incurable disease. EMR for Barrett's with HGD or IMC is performed by multiband or cap mucosectomy and provides technical and long-term treatment success rates for eradication of neoplasia of 97% and 87% to 95%, respectively,[11-13] with early major adverse event rates of 1.5% to 4.7%.[13-19] Complete eradication of the Barrett's mucosa is indicated because advanced neoplasia may be multifocal and can occur within flat Barrett's epithelium without endoscopic indicators such as nodules or ulceration. Furthermore, the risk of neoplastic progression is increased in the entire Barrett's segment in a patient with focal HGD or IMC, such that complete excision may reduce the risk of the development of metachronous neoplasia. The 2 main treatment options to achieve complete Barrett's eradication are EMR and radiofrequency ablation (RFA).

Complete excision is the criterion standard for mucosal neoplasia of the GI tract, with the advantages of complete histology and the clinical certainty of total excision.[20-23] However, complete Barrett's excision (CBE) is limited by esophageal stricture formation occurring in 17% to 88%.[13,16,22,23] The risk of stricture formation relates to the circumference and length of mucosal resection,[19,24,25] and is greatest with resections involving more than 75% of the esophageal circumference or more than 3 cm of mucosal length. Performing a multiple-staged resection can mitigate this, but the esophageal scarring and distortion after a partial resection makes the subsequent procedure technically more difficult and may impede CBE.

There is no proven treatment to prevent post-EMR stricture formation, and identification of a safe and effective method may result in a paradigm shift in the management of Barrett's neoplasia. In this prospective, investigator-initiated study, we evaluated a novel solution of prophylactic, temporary esophageal stenting that may allow single-stage resection to achieve CBE. Our hypotheses are that (1) prophylactic fully covered esophageal stent insertion reduces the risk of post-CBE strictures and (2) single-stage CBE for short-segment circumferential Barrett's with HGD or IMC effectively eradicates Barrett's neoplasia and the Barrett's segment from which it arises.

MATERIALS AND METHODS

Institutional review board approval was obtained, and the study was registered (ClinicalTrials.gov: NCT01554280). All coauthors had access to the study data and reviewed and approved the final manuscript.

Participants

Consecutive patients were recruited who met the following inclusion criteria: (1) circumferential Barrett's esophagus; (2) the circumferential extent and total length of Barrett's was 3 cm or less (Prague classification $\leq$C3) and 5 cm or less (Prague classification $\leq$M5), respectively; (3) had biopsy-confirmed HGD or IMC; and (4) were 18 to 80 years old. Patients were excluded if they had (1) noncircumferential (C0) or long-segment Barrett's esophagus ($>$C3 or $>$M5, or both); (2) no dysplasia, LGD, or submucosal invasive disease (T1b or higher); (3) a tight peptic stricture impeding resection; or (4) medical comorbidities precluding repeat endoscopies. Written informed consent was obtained from all patients before enrollment in the study.

Treatment protocol

Endoscopy was performed by 3 proceduralists (M.J.B., S.J.W., E.Y.L.) and advanced endoscopy fellows under their direct supervision. The entire Barrett's segment was carefully examined by using high-definition white-light endoscopy and narrow-band imaging with dual-focus endoscopes (Olympus HQ190; Olympus, Tokyo, Japan). If endoscopic features of advanced neoplasia such as nodules and depressed areas were seen (Fig. 1A), focal EMR to exclude submucosal invasive disease was performed. If submucosal invasive disease was excluded on histology review, CBE by multiband mucosectomy (Duette; Cook Medical, Winston-Salem, NC) with same-day discharge was performed 2 weeks later (Fig. 1B and Fig. 1C). All resections were performed without submucosal injection by using a microprocessor-controlled electrosurgical generator (ERBE VIO 300; ERBE, Tübingen, Germany). Resection commenced at the palisading vessels of the gastroesophageal junction distally and extended to remove a 2-mm rim of normal esophageal squamous mucosa proximally. The aim was to perform a confluent Barrett's resection. A fully covered self-expandable metal stent (NITI-S Beta, Taewoong Medical, Seoul, South Korea) was inserted with fluoroscopic assistance 10 days after CBE. The stent is Australian Therapeutic Goods Administration approved and has 2 proximal silicone-coated flares with a diameter of 30 mm, which are designed to reduce distal stent migration. The distal 5 cm has a diameter of 22 mm and is cylindrical and coated with polytetrafluoroethylene (Fig. 1D). The stent was deployed to cross the gastroesophageal junction with a cuff of 1 cm within the stomach and the distal 5 cm placed within the mucosal resection defect with the aim to prevent stricture formation. Patients were monitored for 4 hours in recovery and then discharged home on a long-term oral proton pump inhibitor twice daily and 2 weeks of 1 g oral sucralfate 4 times daily. The