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Prophylactic Endoscopic Coagulation to Prevent Bleeding After Wide-Field Endoscopic Mucosal Resection of Large Sessile Colon Polyps

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BACKGROUND & AIMS: **Clinically significant postendoscopic mucosal resection bleeding (CSPEB) is the most frequent significant complication of wide-field endoscopic mucosal resection (WF-EMR) of advanced mucosal neoplasia (sessile or laterally spreading colorectal lesions > 20 mm). CSPEB requires resource-intensive management and there is no strategy for preventing it. We investigated whether prophylactic endoscopic coagulation (PEC) reduces the incidence of CSPEB.**

METHODS: **We performed a prospective randomized controlled trial of 347 patients (mean age, 67.1 y; 55.3% with proximal colonic lesions) undergoing WF-EMR for advanced mucosal neoplasia at 3 Australian tertiary referral centers. Patients were assigned randomly (1:1) to groups receiving PEC (n = 172) or no additional therapy (n = 175, controls). PEC was performed with coagulating forceps, applying low-power coagulation to nonbleeding vessels in the resection defect. CSPEB was defined as bleeding requiring admission to the hospital. The primary end point was the proportion of CSPEB.**

RESULTS: **Patients in each group were similar at baseline. CSPEB occurred in 9 patients receiving PEC (5.2%) and 14 controls (8.0%; $P = .30$). CSPEB was associated significantly with proximal colonic location on multivariate analysis (odds ratio, 3.08; $P = .03$). Compared with the proximal colon, there was a significantly greater number (3.8 vs 2.1; $P = .002$) and mean size (0.5–1 vs 0.3–0.5 mm; $P = .04$) of visible vessels in the distal colon.**

CONCLUSIONS: **PEC does not significantly decrease the incidence of CSPEB after WF-EMR. There were significantly more and larger vessels in the WF-EMR mucosal defect of distal colonic lesions, yet CSPEB was more frequent with proximal colonic lesions. ClinicalTrials.gov NCT01368731.**

Keywords: Colonoscopy; Colonic Polyps; Postpolypectomy; Prevention.

Large laterally spreading and sessile colonic lesions 20 mm or larger (advanced mucosal neoplasia [AMN]) are precursors to invasive colorectal cancer, a leading cause of cancer-related morbidity and mortality worldwide.[1] As a safe and cost-effective ambulatory day-only procedure, wide-field endoscopic mucosal resection (WF-EMR) progressively is replacing surgery as the preferred treatment for these lesions.[2,3] Postprocedure bleeding is the most common significant complication of WF-EMR. Clinically significant post-EMR bleeding (CSPEB) is defined as any bleeding occurring after the completion of the procedure necessitating emergency room presentation, hospitalization, or re-intervention (either repeat endoscopy, angiography, or surgery).[4] The rate of CSPEB after an uneventful WF-EMR of AMN is 7% overall,[5–7] and approaches 12% in the proximal colon.[4,6] CSPEB may be life-threatening and requires resource-intensive management.[8] Establishing an effective, safe, and cost-effective intervention to reduce CSPEB is an important milestone in improving

Abbreviations used in this paper: **AMN, advanced mucosal neoplasia; CSPEB, clinically significant postendoscopic mucosal resection bleeding; PEC, prophylactic endoscopic coagulation; WF-EMR, wide-field endoscopic mucosal resection.**

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the safety outcomes of WF-EMR. In addition, because of the emergence of colorectal cancer screening programs, AMN is being detected more frequently and thus WF-EMR is becoming more commonplace. Currently, there is no proven effective therapy in the prevention of CSPEB after WF-EMR.

The WF-EMR resection defect often contains numerous blood vessels of various sizes that logically are presumed to cause or contribute to subsequent CSPEB. Observational data have shown that prophylactic endoscopic coagulation (PEC) is effective in preventing bleeding after endoscopic resection of superficial neoplastic lesions in the upper gastrointestinal tract[9] and the technique thus has become a fundamental component of the treatment procedure. We performed a prospective randomized controlled trial to evaluate the safety and efficacy of PEC in the prevention of CSPEB after WF-EMR for colorectal AMN.

Methods

Trial Design

This was a prospective multicenter study with balanced randomization (1:1) conducted at 3 Australian tertiary referral centers. The study had institutional ethics board approval (HREC2010/11/4.12(3155) AU RED) and was registered (ClinicalTrials.gov Number NCT01368731). It was investigator-initiated and received no external funding. All authors had access to the study data and reviewed and approved the final manuscript.

Participants

Patients referred for WF-EMR of AMN (colorectal sessile or laterally spreading lesions $\geq$ 20 mm) were enrolled. Written informed consent was obtained from each patient on the day of the procedure.

Study Setting and Conduct

Patients were asked to cease antiplatelet agents 7 days before, and recommence them 5 days after, the procedure. Management of anticoagulant therapy was standardized in accordance with current guidelines,[10] with patients advised to cease warfarin 4 doses before WF-EMR. Warfarin was recommenced on the day after WF-EMR.

The following exclusion criteria applied at the time of colonoscopy: lesion size less than 20 mm, Paris classification 0-Ip appearance, suspected invasive disease, WF-EMR of multiple lesions in 1 session, incompletely resected lesion, or muscularis propria injury (suspected or confirmed). Patients with the uncommon occurrence of major intraprocedural bleeding also were excluded because other interventions for hemostasis are required (clips, epinephrine injection) and may act as confounders. Patients with a bleeding diathesis or those taking warfarin within 4 doses of the procedure also were excluded.

All WF-EMR procedures were performed by a study investigator or a senior therapeutic endoscopy fellow under their direct supervision. All consultant endoscopists have extensive tertiary-level WF-EMR experience. They had performed PEC routinely before the study on an ad hoc basis for lesions thought to be at high risk of CSPEB. Colonoscopy was performed using a high-definition Olympus 180 or 190 series variable-stiffness colonoscope (Q180/190 PCF/CF; Olympus, Tokyo, Japan). The lesion assessment and WF-EMR technique was standardized across the 3 centers and has been described previously in detail.[11,12] The injection solution consisted of 1 mL of methylene blue or 0.4% indigo carmine and 1 mL of 1:10,000 epinephrine combined with 8 mL of succinylated gelatin (Gelofusine; B. Braun, Bella Vista, Australia) solution.[13,14]

In all cases the lesion was removed using microprocessor-controlled current (VIO 300D Endocut Q Effect 3; ERBE Electromedizin, Tübingen, Germany). Standardized assessment of the resection defect included evaluation of the number, size, and presence of herniation of blood vessels, as well as fibrosis in the resection defect. Assessment of vessel and lesion size was estimated against the known diameter of snares used during the procedure (Figure 1*A*). Herniation of vessels was defined as a vertical protrusion of the vessel above the submucosal connective tissue within the resection defect, without overlying connective tissue (Figure 1*B*).

Persistent intraprocedural bleeding (significant oozing or pulsatile bleeding for >60 seconds despite

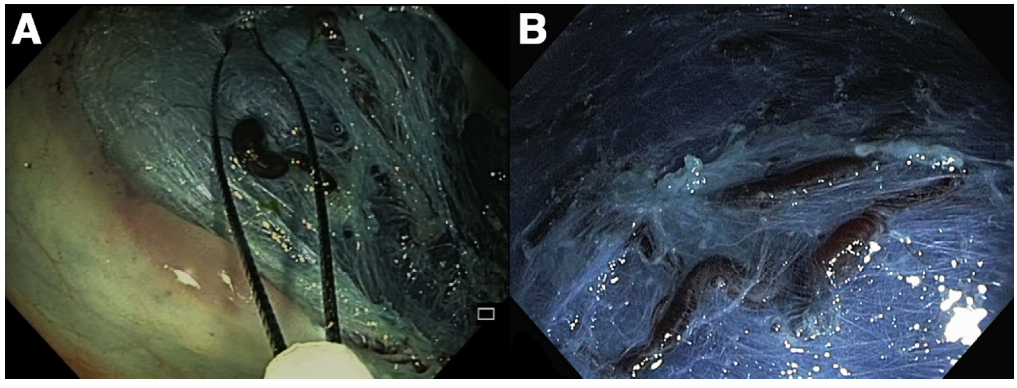

Figure 1. (*A*) Assessment of vessel and lesion size was estimated against the known diameter of snares used during the procedure. (*B*) Herniation of vessels: this was defined as a vertical protrusion of the vessel above the submucosal connective tissue within the resection defect.