Adenoma recurrence after piecemeal colonic EMR is predictable: the Sydney EMR recurrence tool CME

David J. Tate, MA (Cantab), MBBS, MRCP,[1,2] Lobke Desomer, MD,[1] Amir Klein, MD,[1] Gregor Brown, MBBS, PhD, FRACP,[3,4] Luke F. Hourigan, MBBS, FRACP,[5,6] Eric Y. T. Lee, MBBS (Hons), FRACP,[1] Alan Moss, MBBS (Hons), FRACP,[7,8] Donald Ormonde, MBBS, FRACP, PhD,[9] Spiro Raftopoulos, MBBS, FRACP,[9] Rajvinder Singh, MBBS, MRCP, MPhil, FRACP,[10] Stephen J. Williams, MBBS, FRACP,[1] Simon Zanati, MBBS, FRACP,[3,7] Karen Byth, PhD,[11] Michael J. Bourke, MBBS, FRACP[1,2]

Sydney, New South Wales City, Province, Australia

Background and Aims: EMR is the primary treatment of large laterally spreading lesions (LSLs) in the colon. Residual or recurrent adenoma (RRA) is a major limitation. We aimed to identify a robust method to stratify the risk of RRA.

Methods: Prospective multicenter data on consecutive LSLs ≥20 mm removed by piecemeal EMR from 8 Australian tertiary-care centers were included (September 2008 until May 2016). A logistic regression model for endoscopically determined recurrence (EDR) was created on a randomly selected half of the cohort to yield the Sydney EMR recurrence tool (SERT), a 4-point score to stratify the incidence of RRA based on characteristics of the index EMR. SERT was validated on the remainder of the cohort.

Results: Analysis was performed on 1178 lesions that underwent first surveillance colonoscopy (SC1) (median 4.9 months, interquartile range [IQR] 4.9-6.2). EDR was detected in 228 of 1178 (19.4%) patients. LSL size ≥40 mm (odds ratio [OR] 2.47; $P < .001$), bleeding during the procedure (OR 1.78; $P = .024$), and high-grade dysplasia (OR 1.72; $P = .029$) were identified as independent predictors of EDR and allocated scores of 2, 1, and 1, respectively to create SERT. Lesions with SERT scores of 0 (SERT = 0) had a negative predictive value of 91.3% for RRA at SC1, and SERT was shown to stratify RRA to specific follow-up intervals by using Kaplan Meier curves (log-rank $P < .001$).

Conclusions: Guidelines recommend SC1 within 6 months of EMR. SERT accurately stratifies the incidence of RRA after EMR. SERT = 0 lesions could safely undergo first surveillance at 18 months, whereas lesions with SERT scores between 1 and 4 (SERT 1-4) require surveillance at 6 and 18 months. (Clinical trial registration number: NCT01368289.) (Gastrointest Endosc 2017;85:647-56.)

(footnotes appear on last page of article)

Wide-field EMR has become the primary treatment for large laterally spreading lesions (LSLs) in the colon. As a day case procedure, it has significant cost[1] and morbidity benefits over surgery, and modeling indicates that it is also safer.[2] However, residual or recurrent adenoma (RRA) and the necessity for scheduled follow-up remain significant limitations.

Previously published data show RRA rates of 10% to 55%[3] after EMR. In the largest prospective multicenter series to date, a 16.0% recurrence rate was observed at first surveillance colonoscopy (SC1). Late recurrence was observed in 4.0%. Lesion size ≥40 mm and bleeding during the procedure requiring endoscopic control were shown to be independent predictors of RRA at SC1.[4] In other series, piecemeal EMR has been an independent risk factor for RRA at first surveillance, with rates as low as 3% quoted for en bloc resection.[5]

Current guidelines recommend first follow-up colonoscopy at 4 to 6 months[6,7] and a second surveillance colonoscopy (SC2) at a subsequent interval after piecemeal EMR. As the technique of EMR has been steadily improved and rates of recurrence have fallen, it now seems logical to move to staged surveillance procedures depending on defined risk factors for individual patients. Because RRA is often diminutive, without advanced histologic grade and being readily amenable to endoscopic treatment,[8] there may be a low-risk population that does not benefit from SC1 within 6 months of the initial EMR. This approach may reduce the

burden of EMR on patients and health systems while simultaneously achieving cost savings.

METHODS

Data collection

Data were collected and analyzed within a multicenter prospective observational study of patients referred for EMR of colon LSLs ≥20 mm performed at 8 Australian academic tertiary-care referral centers from September 2008 until May 2016 (The Australian Colonic EMR Resection Study, Clinicaltrials.gov NCT01368289). There were no exclusions to enrollment. Institutional review board approval was obtained at each center. This study involves long-term follow-up of the original cohort of 479 patients[9] as well as additional consecutively included patients until May 2016.

Data collection at the initial EMR included patient, lesion, and procedural characteristics. Postprocedural data including delayed adverse events, and results of follow-up were collected by structured telephone interviews at 14 days after the index procedure and at the time of each surveillance colonoscopy. Delayed bleeding was defined as bleeding after the procedure that required hospital admission or reintervention. All authors had access to the study data and reviewed and approved the final manuscript.

EMR procedure

EMR procedures were performed by senior endoscopists with extensive EMR experience or by a senior endoscopy fellow under direct supervision by a senior endoscopist. Written informed consent was obtained from all patients. Split-dose bowel preparation was used. Intravenous sedation was with a combination of fentanyl, midazolam, and propofol. Insufflation of the colon was initially with air, moving to carbon dioxide in August 2010.[10]

Colonoscopy was performed by using Olympus 180 or 190 series high-definition variable-stiffness colonoscopes (180/190 PCF/CF; Olympus, Tokyo, Japan). Lesion assessment was performed with high-definition white light and narrow-band imaging. Size of lesions was determined with reference to an open snare of known diameter. Patients were excluded if they were referred for surgery at the time of the initial EMR, based on morphology or review of histopathology. A standardized and previously described inject-and-resect EMR technique[11] was used. Figure 1 shows an example of the EMR of a near circumferential LSL in the rectum. Most cases used a microprocessor-controlled electrosurgical generator (Endocut effect 3, VIO 300D; ERBE Elektromedizin, Tübingen, Germany)[12] with fractionated current. The submucosal injectate was made up of normal saline solution until 2010 when it was replaced with succinylated gelatin (Gelofusine; B. Braun Australia Pty Ltd, Bella Vista, Australia).[13] The fluid was dyed with indigo carmine blue (80 mg/500 mL solution), and adrenaline was added to achieve a final solution of 1:100,000. Lesions resected en bloc were excluded. Bleeding during the procedure was treated with snare tip soft coagulation (ERBE, effect 4, 80 W) and was recorded as present if endoscopic control was required. Complete snare excision was the goal in all cases. If this was not possible, ablative thermal therapy was used. Before 2012, argon plasma coagulation was used as a salvage ablative therapy in cases of incomplete excision. Subsequently, cold forceps avulsion followed by snare tip soft coagulation to the avulsion bed has been used. Deep injury was defined as types II to V within the Sydney Deep Mural Injury Classification system.[14] Pathologists who were specialists in gastroenterology at the individual centers reviewed all histologic specimens.

After EMR, patients were observed for 4 hours and discharged home if well. A clear fluid diet was advised until the next morning.

Follow-up

Follow-up data were collected from patients eligible for SC1 at a planned interval of 4 to 6 months. Time to longest follow-up and any associated recurrence after SC1 were recorded if available. SC2 was performed at a planned interval of 12 months (ie, 18 months after the original EMR) and SC3 at a planned interval of 18 months (ie, 36 months after the original EMR). Later surveillance was conducted in accordance with published international surveillance guidelines for the particular patient.[7] Analysis was performed on a per-patient basis, with only the largest lesion from each patient included to avoid the problem of potential bias associated with correlated observations for a single patient. Patients with <3 months of follow-up time (including lesions that underwent 2-stage EMR) were excluded. Between May 2013 and January 2016, patients enrolled and randomized to the active arm of the SCAR study (snare tip soft coagulation to prevent recurrence after colon EMR, NCT02000141) were excluded. Patients with missing data were regarded as lost to follow-up.

All EMR scars were evaluated endoscopically at SC1 and at further follow-up if undertaken. The primary endpoint of the study was endoscopically determined recurrence (EDR), defined as the presence of tissue suspicious for adenoma under high-definition white light and/or narrow-band imaging. When there was any doubt as to the presence of EDR, biopsy specimens of the EMR scar were taken to document the presence or absence of histologic recurrence (histologically determined recurrence [HDR]). Late recurrence was defined as RRA that occurred at a surveillance procedure ≥16 months after the index EMR. Detected RRA, once sampled, was excised by snare or, if this was not possible, removed by cold forceps avulsion followed by snare tip soft coagulation.