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Simple optical evaluation criteria reliably identify the post-endoscopic mucosal resection scar for benign large non-pedunculated colorectal polyps without tattoo placement

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ABSTRACT

Background Recognition of the post-endoscopic mucosal resection (EMR) scar is critical for large (≥ 20 mm) non-pedunculated colorectal polyp (LNPCP) management. The utility of intraluminal tattooing to facilitate scar identification is unknown.

Methods We evaluated the ability of simple easy-to-use optical evaluation criteria to detect the post-EMR scar, with or without tattoo placement, in a prospective observational cohort of LNPCPs referred for endoscopic resection. The primary outcome was scar identification, further stratified by lesion size (20–39 mm, ≥ 40 mm) and histopathology (adenomatous, serrated).

Results 1023 LNPCPs underwent both successful EMR and first surveillance colonoscopy (median size 35 mm, IQR 30–50 mm); 124 (12.1 %) had an existing tattoo or a tattoo placed at the index EMR. The post-EMR scar was identified in 1020 patients (99.7 %). The presence of a tattoo did not affect scar identification (100.0 % vs. 99.7 %; $P > 0.99$). There was no difference for LNPCPs 20–39 mm, LNPCPs ≥ 40 mm, adenomatous LNPCPs, and serrated LNPCPs (all $P > 0.99$).

Conclusions The post-EMR scar can be reliably identified with simple easy-to-use optical evaluation criteria, without the need for universal tattoo placement.

Introduction

Surveillance colonoscopy is critical to managing large (≥ 20 mm) non-pedunculated colorectal polyps (LNPCPs) after endoscopic mucosal resection (EMR) as it allows for the identification and treatment of residual or recurrent polypoid tissue [1, 2]. This is predicated on recognizing the post-EMR scar. To facilitate its identification, sterile carbon particle suspension can be used to create an intraluminal tattoo. However, it is not biologically inert and can precipitate clinically relevant adverse outcomes [3–5].

Although current consensus guidelines provide recommendations, they are largely based on expert opinion, with no evidence available on whether tattoo placement facilitates scar identification [3, 4]. Therefore, we evaluated the ability of simple easy-to-use optical evaluation criteria to detect the post-EMR scar [6], with or without tattoo placement, in a prospective observational cohort of LNPCPs referred for endoscopic resection.

Method

The Australian Colonic Endoscopic Resection (ACE) study

The Australian Colonic Endoscopic Resection (ACE) study (clinicaltrials.gov identifier: NCT01368289) is a prospectively collected, multicenter, observational cohort of consecutive patients referred for the management of LNPCPs ≥ 20 mm (July 2008 to present). Center-specific Institutional Review Board approval is

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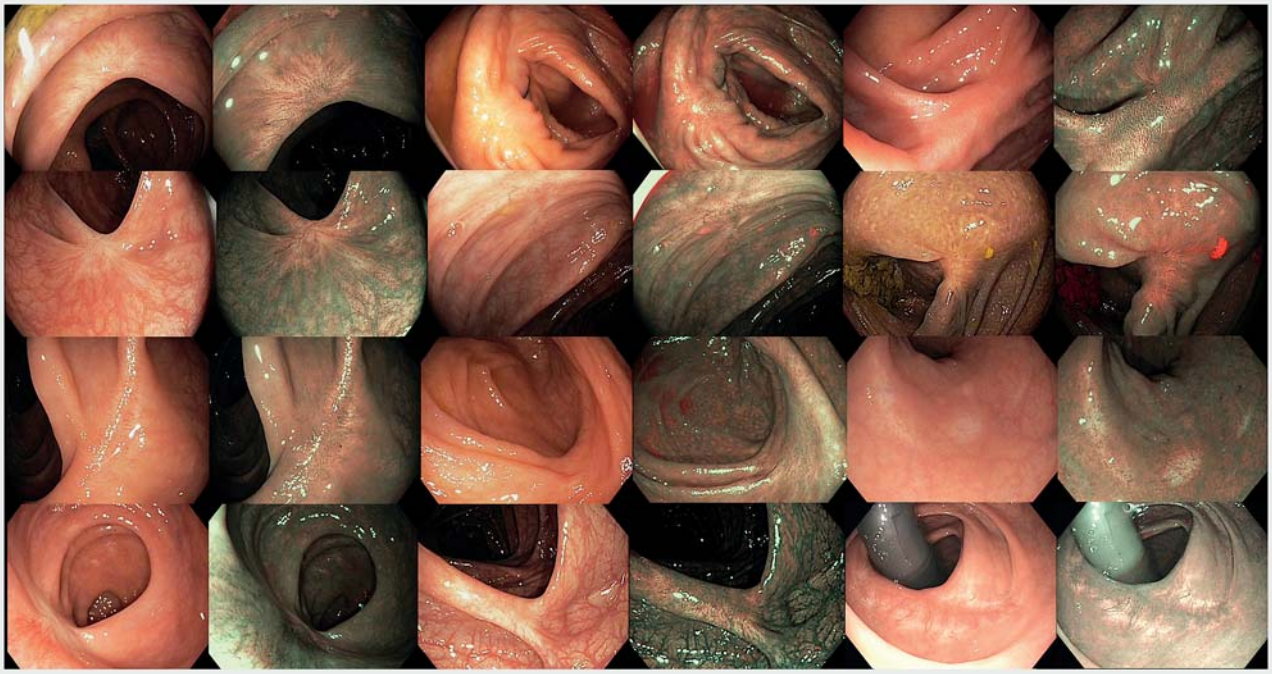

▶ **Fig. 1** Example images of post-endoscopic mucosal resection scars on high definition white-light endoscopy and narrow-band imaging.

maintained at each center. Written informed consent is obtained from each patient prior to study participation.

Consecutive LNPCPs (July 2008 to October 2019) that underwent successful EMR and first surveillance colonoscopy (SC1), as recommended at 6 months after the index EMR, at one ACE site were included for this analysis.

Endoscopic mucosal resection technique

A standardized, previously described, inject and resect EMR technique was used [7, 8]. All endoscopic procedures were performed by a study investigator (an accredited gastroenterologist with advanced training and an established tertiary referral practice in colorectal EMR) or a senior interventional endoscopy fellow under supervision. Antiplatelet and anticoagulation medications were withheld pre-procedure, in accordance with consensus recommendations [9].

Currently, all colorectal EMRs are performed using high definition Olympus 190 series variable stiffness colonoscopes (Olympus, Tokyo, Japan). Carbon dioxide is used for insufflation [10]. After lesion identification, optical evaluation under high definition white-light endoscopy and narrow-band imaging (NBI) is performed to exclude features of submucosal invasive cancer (SMIC). In a systematic fashion, a submucosal cushion is created with injection of succinylated gelatin (Gelofusine; B. Braun, Bella Vista, Australia) with 0.4% indigo carmine and 1:100 000 epinephrine. A microprocessor-controlled generator (ERBE VIO; Endocut Q, effect 3; ERBE, Tübingen, Germany) is used, with snare excision being performed [8].

After complete resection of the LNPCP, the defect is carefully examined to ensure no polypoid tissue remains and to assess for deep mural injury (DMI) [11]. Areas of significant injury (DMI III–V) are subsequently treated by mechanical clip closure. Thermal ablation of the resection margin to mitigate the risk of recurrence is performed using snare-tip soft coagulation (ERBE VIO; Soft coagulation, 80 W, effect 4; ERBE) to create a rim of ablated tissue of 2–3 mm. Clinically significant intraprocedural bleeding is treated with coagulation forceps or mechanical hemostasis. A tattoo may be placed distal to the EMR defect as deemed appropriate by the proceduralist. Resection specimens are collected and evaluated by specialist gastrointestinal pathologists. Where appropriate, histopathology is confirmed with surgical specimen evaluation.

Surveillance colonoscopy

Prior to SC1, the report and images from the index EMR are reviewed, with the location and colonic segment of the resected LNPCP being noted. The relationship to relevant structures such as haustral folds are noted, where appropriate. Once the colonoscope is in the expected vicinity of the post-EMR scar, patients undergo standardized evaluation using high definition white-light endoscopy and NBI. After identification of the scar, previously reported, simple, and easy-to-use optical evaluation criteria are used for endoscopic confirmation [6]. In detail, the scar may be identified as a pale area with disruption of the normal colonic surface microvasculature and pit pattern, and there may be convergence of the surrounding mucosal folds (▶ **Fig. 1**). Closer inspection of a bland scar with NBI typically demonstrates a non-neoplastic pit pattern, as opposed to the neoplastic pit pattern seen with residual or recurrent polypoid tissue. Biopsies are routinely performed.

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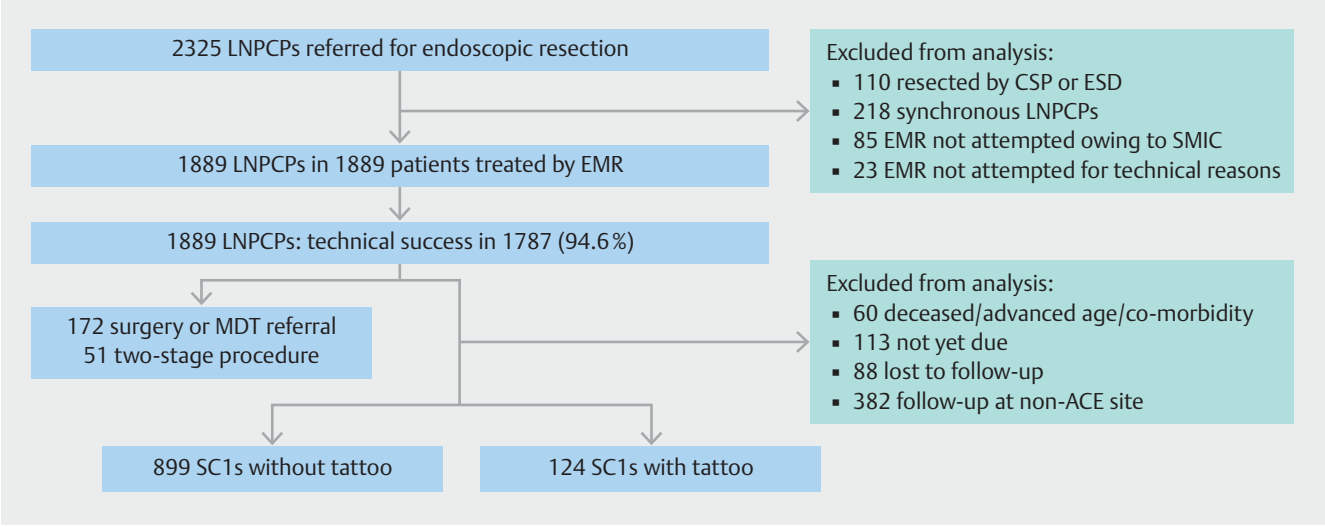

▶ **Fig. 2** Flow Diagram of consecutive large non-pedunculated colorectal polyps referred for endosocpic resection
ACE, Australian Colonic Endoscopic Resection; CSP, cold snare polypectomy; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; LNPCP, large non-pedunculated colorectal polyp; MDT, multidisciplinary team; SC1, surveillance colonoscopy 1; SMIC, submucosal invasive cancer.

Statistical analysis

Prospectively collected data included: (1) patient characteristics, including age, sex, and American Society of Anesthesiologists (ASA) classification; (2) lesion characteristics, including size, location, morphology, surface granularity, Kudo pit pattern, histopathology, and tattoo placement; and (3) procedure outcomes, including technical success, periprocedural adverse events, recurrence, and referral for surgery.

The primary outcome was scar identification, stratified by the presence of a tattoo. Further stratifications by lesion size (20–39 mm, ≥ 40 mm) and histopathology (adenomatous, serrated) were performed.

SPSS version 26.0 (IBM, Armonk, New York, USA) was used for data analysis. Variables were analyzed per participant. If two or more eligible lesions were identified in a single participant, the largest lesion was selected for analysis. Continuous variables were summarized as median (interquartile range [IQR]). Categorical variables were summarized as frequencies (%). All analyses were exploratory and two-tailed tests with a 5 % significance level were used throughout. Fisher exact tests were used to test for associations between categorical variables.

Results

Between July 2008 to October 2019, 1023 LNPCPs in 1023 patients underwent both successful EMR and SC1 (▶ **Fig. 2**). The median patient age was 69 years (IQR 62–75 years) and 535 (52.3 %) were men (▶ **Table 1**). The median lesion size was 35 mm (IQR 30–50 mm). Of the screening colonoscopies performed, 124 (12.1 %) were for lesions that had an existing tattoo or had had a tattoo placed at the index EMR. Of these, 12 (9.7 %) were placed at the time of index EMR because of difficult positioning secondary to looping (n = 4), a redundant colon (n = 4), or for unclear reasons (n = 4).

Surveillance colonoscopy

The median time to SC1 was 5 months (IQR 4–6 months). The post-EMR scar was successfully identified in 1020 patients (99.7 %). In three patients (0.3 %), the scar was not identified, which in all cases was attributed to poor bowel preparation, with the scar subsequently being confirmed on repeat surveillance colonoscopy. In all cases where biopsies were taken (n = 769), histological analysis was either consistent with the presence of a bland post-EMR scar (n = 655) or showed the presence of residual or recurrent polypoid tissue (n = 114).

There was no difference in successful scar identification between patients with and without a tattoo (100.0 % vs. 99.7 %; $P > 0.99$). On further stratification, no difference in scar identification was found for LNPCPs 20–39 mm, LNPCPs ≥ 40 mm, serrated LNPCPs, and adenomatous LNPCPs (all $P > 0.99$).

A second surveillance colonoscopy (SC2) was performed for 67 patients within the ACE site, at a median time of 15 months (IQR 12–21 months) following EMR. Of these, nine (13.4 %) had received a prior tattoo. In all 67 cases, the post-EMR scar was identified.

Discussion

Although tattoo placement is commonly used to facilitate post-EMR scar identification, the incremental benefit is largely unknown. Moreover, it can lead to adverse outcomes including: (1) diffusion of the tattoo under the resection site, which can preclude residual or recurrent polypoid tissue management; (2) peritonitis after transmural injection; (3) inaccurate lesion localization, specifically during laparoscopic surgery, owing to inappropriate tattoo placement; (4) increased surgical complexity for rectal LNPCPs, owing to mesorectal spillage; and (5) tumor seeding [3–5]. This study demonstrates that scar identi-

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▶ **Table 1** Characteristics of the 1023 patients and their large non-pedunculated colorectal polyps that were treated by endoscopic mucosal resection with a surveillance colonoscopy performed within 6 months.

	No tattoo (n = 899)	Tattoo (n = 124)	Overall (n = 1023)
Age, median (IQR), years	69 (62–75)	70 (63–76)	69 (62–75)
Sex, male, n (%)	468 (52.1)	67 (54.0)	535 (52.3)
Size, median (IQR), mm	40 (30–50)	35 (25–40)	35 (30–50)
Location, n (%)			
▪ Rectosigmoid	241 (26.8)	24 (19.4)	265 (25.9)
▪ Proximal	658 (73.2)	100 (80.6)	758 (74.1)
Paris classification, n (%)[1]			
▪ 0-Is	64 (7.1)	8 (6.5)	72 (7.1)
▪ 0-IIa	501 (55.9)	72 (58.1)	573 (56.1)
▪ 0-IIb	37 (4.1)	13 (10.5)	50 (4.9)
▪ 0-IIa + Is	276 (30.8)	27 (21.8)	303 (29.7)
▪ Any 0-IIc	19 (2.1)	4 (3.2)	23 (2.3)
Granularity[2], n (%)[3]			
▪ Granular	568 (65.1)	53 (42.7)	621 (62.3)
▪ Non-granular	215 (24.7)	61 (49.2)	276 (27.7)
▪ Mixed	49 (5.6)	6 (4.8)	55 (5.5)
▪ Serrated	40 (4.6)	4 (3.2)	44 (4.4)
Histopathology, n (%)			
▪ Adenomatous	750 (83.4)	108 (87.1)	858 (83.9)
▪ Serrated	130 (14.5)	16 (12.9)	146 (14.3)
▪ Other	19 (2.1)	0 (0.0)	19 (1.9)

IQR, interquartile range.
[1] Morphology not classified for two participants.
[2] $P<0.001$ when comparing tattoo with no tattoo.
[3] Granularity not classified for 27 participants

fication did not significantly differ between patients with and without tattoo placement. By reviewing the index EMR reports and photodocumentation, including the LNPCP location and colonic segment, scars were readily identified and then confirmed using simple easy-to-use optical evaluation criteria [6]. Given the potential adverse outcomes associated with the sterile carbon particle suspension, tattoo placement should be reserved for select lesions, such as those with suspected SMIC, difficult positioning, or bowel redundancy.

With the widespread availability of high definition colonoscopes, it is now the expectation that competent endoscopists reliably detect diminutive colorectal polyps. To achieve this, skill enhancement programs, which include teaching about the optical characteristics of adenomatous and serrated polypoid tissue, have been developed. The process of identifying a post-EMR scar is no different; for LNPCPs, this should arguably be easier given their size (▶ **Fig. 1**). However, an emphasis is currently placed on teaching the technical aspects of high quality EMR and less on the periprocedural management of LNPCPs, including scar identification. Skill enhancement programs on the gamut of LNPCP management, informed by evidence-based quality indicators in EMR, are therefore needed [12].

This study is not without limitations. It is a single-center analysis, from a center with recognized expertise in minimally invasive endoscopic resection techniques. Therefore, confirmation of these findings is needed. The majority of tattoos had been placed by the referring physician or surgeon. As it was not possible to determine the reasons for tattoo placement, the generalizability of our results are reduced. Moreover, this study did not evaluate alternative endoscopic resection techniques, including endoscopic submucosal dissection and piecemeal cold-snare resection.

In conclusion, this study shows that, at a center that is expert in minimally invasive endoscopic resection techniques, the post-EMR scar can be reliably identified and confirmed with simple easy-to-use optical evaluation criteria. In the era of quality assurance in colonoscopy, skill enhancement programs on LNPCP management must incorporate training in post-EMR scar identification. Moreover, this potentially negates the role for universal tattoo placement. Tattooing should be reserved for LNPCPs with suspected SMIC [13] that are either being referred for surgery or being considered for an advanced endoscopic resection technique. Moreover, it may be appropriate in select cases where lesion identification is difficult, such as in the transverse or sigmoid colon where bowel redundancy and loose mesenteric attachments may make re-identification of the resection site challenging.

Clinical trial

Trial Registration: Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au/) | Registration number (trial ID): NCT01368289 | Type of study: Multi-Center Study

Competing interests

Michael J. Bourke has received research support from Olympus, Cook Medical, and Boston Scientific. The remaining authors declare that they have no conflict of interest.

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