Effect of pre-resection biopsy on detection of advanced dysplasia in large nonpedunculated colorectal polyps undergoing endoscopic mucosal resection

GRAPHICAL ABSTRACT

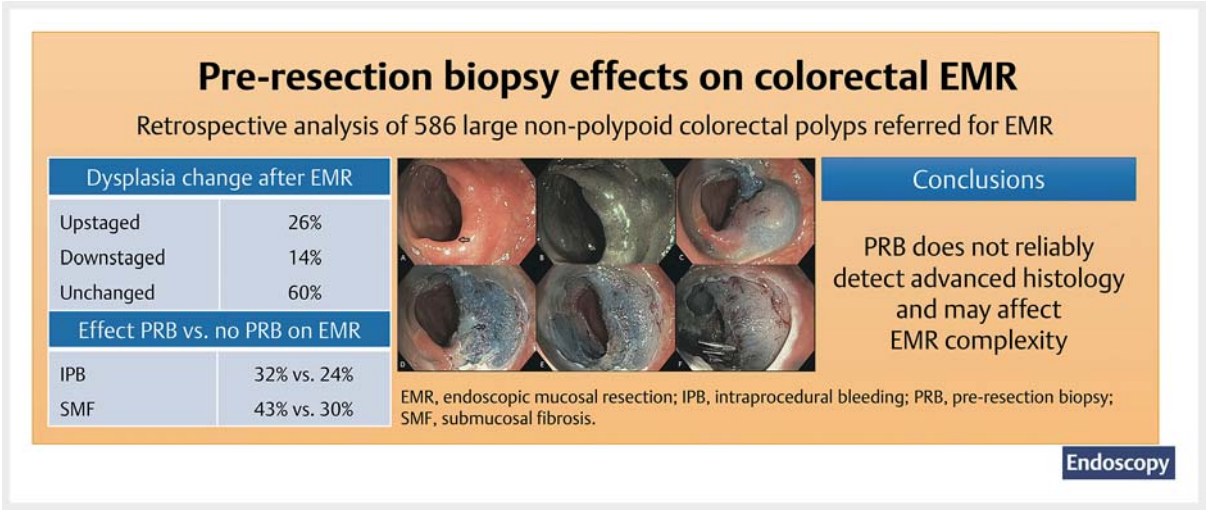

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Table 1 s
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ABSTRACT

Background Pre-resection biopsy (PRB) of large non-pedunculated colorectal polyps (LNPCPs, ≥ 20 mm) is often performed before referral for endoscopic mucosal resection (EMR). How this affects the EMR procedure is unknown.

Methods This was a retrospective analysis of a prospectively collected cohort of patients with LNPCPs referred for EMR between 2013 to 2016 at an Australian tertiary center. Outcomes were differences between PRB and EMR histology, and effects of PRB on the EMR procedure.

Results Among 586 LNPCPs, lesions that underwent PRB were larger (median 35 vs. 30 mm; $P<0.007$), and more commonly morphologically flat or slightly elevated ($P=0.01$) compared with lesions without PRB. PRB histology was upstaged in 26.1 %, downstaged in 13.8 %, and unchanged in 60.1 % after EMR. Sensitivity of PRB was 77.2 % (95 %CI 71.1–82.4) for low grade dysplasia (LGD) and 21.2 % (95 %CI 11.5–35.1) for high grade dysplasia (HGD). Where EMR specimen showed HGD, PRB had detected LGD in 76.9 %. Where

EMR specimen showed cancer, PRB had detected dysplasia only. PRB was associated with more submucosal fibrosis (P = 0.001) and intraprocedural bleeding (P = 0.03). EMR success or recurrence was not affected.

Conclusions Routine PRB of LNPCP did not reliably detect advanced histology and may have affected EMR complexity. PRB should be utilized with caution in guiding endoscopic management of LNPCPs.

Introduction

Large (≥ 20 mm) nonpedunculated colorectal polyps (LNPCP) comprise 2 %–5 % of polyps identified in colorectal cancer screening programs [1]. These lesions are premalignant and can be endoscopically resected. Owing to its efficiency, safety, and cost and clinical effectiveness, endoscopic mucosal resection (EMR) is an established treatment for LNPCPs [2–5]. Pre-resection diagnosis is important in order to optimize treatment decisions, as a subgroup may contain early submucosal invasion and be unsuitable for EMR. Specific endoscopic imaging parameters can be used to assess presence of submucosal invasion in LNPCPs. These include lesion morphology and surface microvascular and pit pattern [6–8]. Routine pre-resection biopsy (PRB) of LNPCP for histology, is also traditionally used. However, whether PRB is useful in guiding treatment decisions has not been established by evidence. Therefore, we sought to assess differences in PRB and EMR specimen histology, and the effect of PRB on EMR outcomes from our center.

Methods

Data collection

Data were collected and analyzed within a prospective observational study of patients referred for EMR of colonic LNPCPs ≥ 20 mm performed at a tertiary care referral center from January 2013 to November 2016 (The Australian Colonic EMR Resection Study, ClinicalTrials.gov NCT01368289). Lesions with prior attempted EMR and incomplete follow-up data were excluded. Institutional review board approval was obtained.

Data collection at initial EMR included patient, lesion, procedural characteristics, and delayed adverse events at 14 days. Presence of PRB was determined by review of colonoscopy and histology reports from the referring endoscopist. These were correlated with the lesion referred for EMR. Specialist gastrointestinal pathologists reviewed all histologic specimens. Dysplasia was graded as absent, low grade (LGD), high grade (HGD), or cancer (submucosal invasion). Follow-up data were collected at planned intervals of 4–6 months and 18 months from index EMR (SC1 and SC2, respectively). All authors had access to the study data and approved the final manuscript.

EMR procedure

EMR procedures were performed by experienced endoscopists or by a senior endoscopy fellow. Written informed consent was obtained from all patients. Split-dose bowel preparation was used. Insufflation of the colon was performed using carbon dioxide.

Colonoscopy was performed using Olympus 190 series high definition colonoscopes (180/190 PCF/CF; Olympus, Tokyo, Japan). Lesion assessment was performed with high definition white-light and narrow-band imaging (NBI). A standardized inject-and-resect EMR technique was used [9–11], using a microprocessor-controlled electrosurgical generator (Endocut effect 3, VIO 300D; ERBE Elektromedizin, Tübingen, Germany) with fractionated current. The submucosal injectate included succinylated gelatin (Gelofusine; B. Braun Australia Pty Ltd, Bella Vista, Australia) [12], indigo carmine blue (80 mg/500 mL solution), and adrenaline diluted to 1:100 000.

Intraprocedural bleeding (IPB) was treated with snare tip soft coagulation (effect 4, 80 W; ERBE,) and defined as present if persisting for ≥ 30 seconds or if requiring endoscopic control [13]. Clinically significant post-EMR bleeding included any bleeding occurring after completion of EMR necessitating emergency room presentation, hospitalization, or reintervention. Muscularis propria injury was suspected when a nonstaining disrupted area was seen within the blue EMR defect [14]. Poorly stained areas were evaluated using topical submucosal chromoendoscopy [15], and treated by clip closure if suspicious for deep mural injury (type III–V) [14]. Procedural success was defined as complete excision of adenomatous tissue. If this was not possible, cold forceps avulsion followed by snare tip soft coagulation to the avulsion bed was performed [16]. After EMR, patients were observed for 4 hours and discharged home if well. A clear fluid diet was advised until the next morning.

Statistical analysis

Statistical analysis was performed using SPSS version 23 (IBM Corp., Armonk, New York, USA) with a two independent samples t test used for continuous variables, and Pearson's chi-squared test or Fisher's exact test for categorical variables. All tests were two sided. Categorical variables were described using counts and percentages (%). Continuous variables were summarized using mean and SD, or median and interquartile range (IQR), as appropriate. A P value of <0.05 was regarded as statistically significant.

Results

Patient population and lesion characteristics

EMR was performed on 742 LNPCPs. Of these, 156 met exclusion criteria, leaving 586 lesions for analysis. PRB was performed on 343 LNPCPs (58.5 %). Mean patient age was 67.5 years, 297 (50.7 %) were male, and median lesion size was 30 mm (SD 13.9 mm). Baseline patient, lesion, and procedural characteristics including lesion size, colonic location, morphology, and adverse events are outlined in ▶ **Table 1**.

▶ **Table 1** Patient cohort characteristics.

	No biopsy (n = 243)	Pre-EMR biopsy (n = 343)	*P*
Patient			
▪ Age, mean (SD), years	67.9 (11.25)	67.2 (12.2)	0.44
▪ Male sex, n (%)	133 (54.7)	164 (47.8)	0.10
Lesion			
▪ Size, median (IQR), mm	30 (15)	35 (20)	**0.007**
Location, n (%)			
▪ Right (hepatic flexure to cecum)	136 (56.0)	164 (47.8)	0.05
▪ Distal to hepatic flexure	107 (44.0)	179 (52.2)	0.05
Morphology, n (%)			
▪ Granular	127 (52.3)	173 (50.4)	0.70
▪ Nongranular	78 (32.1)	107 (31.2)	0.70
▪ Serrated/other	38 (15.6)	63 (18.4)	0.70
▪ Paris Is component present	77 (31.7)	143 (41.7)	**0.01**
▪ Submucosal fibrosis	73 (30.0)	148 (43.1)	**0.001**
▪ Invasive cancer	10 (4.1)	20 (5.8)	0.35
Procedure			
▪ Duration, median (IQR), minutes	20 (20)	25 (25)	0.06
▪ En bloc resection, n (%)	8 (3.3)	17 (5.0)	0.33
▪ IPB, n (%)	57 (23.5)	108 (31.5)	**0.03**
▪ Deep injury*, n (%)	5 (2.1)	8 (2.3)	0.82
▪ Successful EMR, n (%)	237 (97.5)	333 (97.1)	0.74
Adverse events, n (%)			
▪ Delayed bleeding	22 (9.1)	24 (7.0)	0.36
▪ Delayed perforation	1 (0.4)	2 (0.6)	0.77
Follow-up, n/N (%)			
▪ EDR at SC1	33/176 (18.8)	41/251 (16.3)	0.52

EMR, endoscopic mucosal resection; IQR, interquartile range; IPB, intraprocedural bleeding requiring endoscopic control; EDR, endoscopically determined recurrence; SC1, first surveillance colonoscopy.
* Deep injury was defined as target sign or actual hole within the EMR defect.

LNPCPs that underwent PRB were larger than those without PRB (median 35 mm [IQR 20 mm] vs. median 30 mm [IQR 15 mm], respectively; $P<0.007$). A total of 300 LNPCPs were located at, or proximal to the hepatic flexure. Rates of PRB proximal and distal to the hepatic flexure were similar (47.8 % [164/343] vs. 52.2 % [179/343], respectively; $P=0.05$). Flat and slightly elevated lesions were more likely to have undergone PRB than lesions with a nodular (Paris 0-Is) component (58.3 % [200/343] vs. 41.7 % [143/343], respectively; $P=0.01$). There was no significant difference in rates of PRB for granular, nongranular, or serrated lesions (173 [50.4 %] vs. 107 [31.2 %] vs. 63 [18.4 %], respectively; $P=0.70$).

Effect of nontargeted biopsy on EMR procedure

Median procedural duration for lesions with PRB was 25 minutes (IQR 25 minutes) vs. 20 minutes (IQR 20 minutes) for lesions without PRB ($P=0.06$). Submucosal fibrosis occurred more frequently in lesions with PRB than lesions without PRB (43.1 % [148/343] vs. 30.0 % [73/243], respectively; $P=0.001$), but was not significantly associated with the need for more than one modality to complete the resection (16.0 % [55/343] vs. 12.8 % [31/243], respectively; $P=0.27$). Successful EMR was not significantly affected by PRB (97.1 % [333/343] vs. 97.5 % [237/243]; $P=0.74$). En bloc resection rates were also not significantly affected by PRB (5.0 % [17/343] vs. 3.3 % [8/243]; $P=0.33$).

Effect of nontargeted biopsy on EMR adverse events

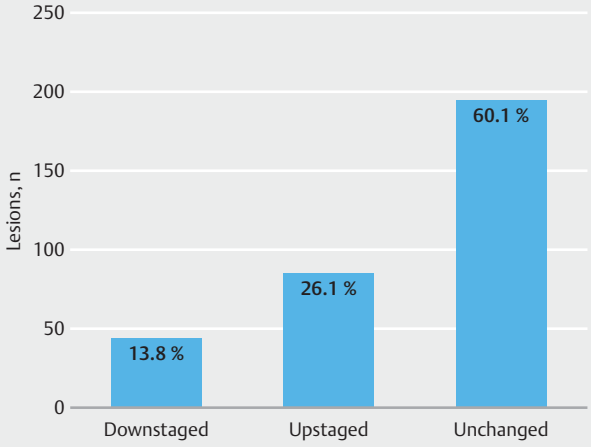
Overall IPB and clinically significant post-EMR bleeding occurred in 165 (28.2%) and 46 (7.8%) of cases, respectively. Treatment modalities of IPB are shown in **Table 1 s** in the online-only supplementary material. PRB was associated with a higher rate of IPB during EMR compared with no PRB (31.5% [108/343] vs. 23.5% [57/243], respectively; $P=0.03$). However, PRB was not associated with significantly increased clinically significant post-EMR bleeding following EMR compared with no PRB (7.0% [24/343] vs. 9.1% [22/243], respectively; $P=0.36$).

Deep mural injury requiring intraprocedural clip closure occurred in eight patients (2.3%) with PRB and in five patients (2.1%) without PRB ($P=0.82$). Delayed perforation occurred in three patients (0.5%), two of whom had PRB. Endoscopically detected adenomatous recurrence at first surveillance colonoscopy (SC1) occurred in 16.3% of cases (41/251) with PRB and 18.8% (33/176) without PRB ($P=0.52$).

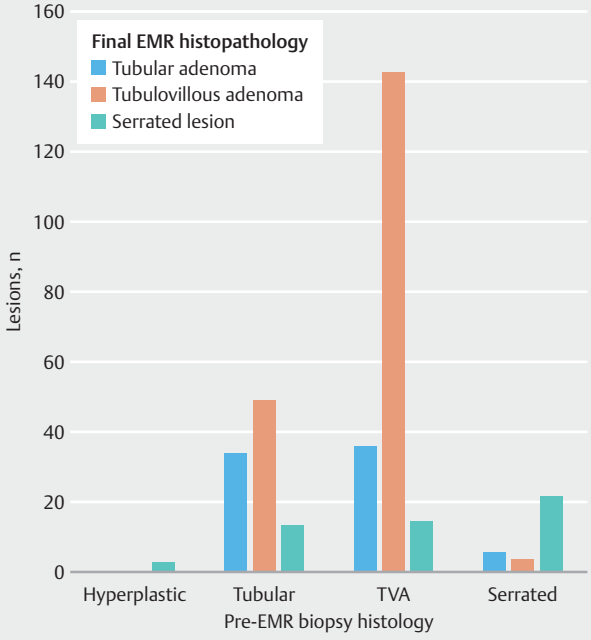
Comparison of PRB and EMR specimen histology

Paired histology results of PRB and post-EMR specimens were available for 326 patients (▶ **Fig. 1**, ▶ **Fig. 2**). Within this patient cohort, PRB found 38 (11.7%) had no dysplasia (sessile serrated lesions), 246 (75.5%) had LGD, and 42 (12.9%) had HGD. In comparison, histology of EMR specimens found 31 (9.5%) had no dysplasia, 224 (68.7%) had LGD, 52 (16.0%) had HGD, and 19 (5.8%) had cancer. With respect to the highest level of dysplasia within the EMR specimen, PRB histology was upstaged in 85 (26.1%), downstaged in 45 (13.8%), and unchanged in 196 (60.1%).

The diagnostic performance of PRB to predict final EMR specimen histology was as follows: sensitivity 77.2% (95%CI 71.1–82.4) for LGD and 21.2% (95%CI 11.5–35.1) for HGD; specificity 28.4% (95%CI 20.2–38.4) for LGD and 88.7% (95%CI 84.2–92.1) for HGD. For the 224 LNPCPs where EMR specimen showed LGD, PRB detected HGD in 26 (11.6%) or no dysplasia in 25 (11.2%). For the 52 LNPCPs where EMR specimen showed HGD, PRB detected LGD in 40 (76.9%) or no dysplasia in 1 (1.9%). For the 19 LNPCPs where EMR specimen showed cancer, PRB detected LGD in 15 (78.9%) and HGD in 4 (21.1%) (▶ **Table 2**).



▶ **Fig. 1** Change in degree of dysplasia on histology after endoscopic mucosal resection.



▶ **Fig. 2** Final endoscopic mucosal resection histology relative to pre-resection biopsy. EMR, endoscopic mucosal resection.

Discussion

EMR is the preferred therapeutic procedure for the majority of nonmalignant LNPCPs. For such lesions, EMR is safe, efficient, and cost-effective with a high rate of cure. Accurate pre-resection lesion assessment to exclude submucosal invasion within LNPCPs is key to successful EMR. This study assessed the effects of PRB on 343 LNPCPs removed by EMR. More than half (58.5%) of the 586 study lesions underwent PRB. Despite the popularity of PRB, our results showed that final specimen histology grade differed from PRB histology in over one in three cases, with the degree of dysplasia being upstaged in the majority of discordant cases (85/130). In practice, EMR is appropriate for all dysplastic lesions, and in this respect, PRB probably did not meaningfully alter management. Post-EMR specimen histology diagnosed 19 cancers (5.8%). For these lesions, PRB did not detect occult malignancy and potentially provided false reassurance of the appropriateness of EMR.

Similar findings of discordance between PRB and EMR specimen histology have been reported in studies assessing EMR of large duodenal lesions [17, 18]. In one study, EMR changed the histology in 30% of cases (upstaged in 27%, downstaged in 3%) compared with PRB [17]. In another study, comparison of the biopsy diagnosis and specimen histology revealed the same diagnosis in 59%, upstaged histology in 36%, and downstaged

▶ **Table 2** Agreement of pre-endoscopic mucosal resection (EMR) nontargeted biopsy with final EMR histopathology.

	EMR specimen most advanced level of cytological dysplasia				Total
	None	LGD	HGD	Cancer	
Biopsy specimen dysplasia level, n (%)					
▪ None	12 (31.6)	**25 (65.8)**	**1 (2.6)**	0 (0)	38
▪ LGD	**18 (7.3)**	173 (70.3)	**40 (16.3)**	**15 (6.1)**	246
▪ HGD	**1 (2.4)**	**26 (61.9)**	11 (26.2)	**4 (9.5)**	42
▪ Cancer	0 (0)	0 (0)	0 (0)	0 (0)	0
Total, n	31	224	52	19	326
Sensitivity, % (95 %CI)	38.7 (22.4–57.7)	77.2 (71.1–82.4)	21.2 (11.5–35.1)		
Specificity, % (95 %CI)	91.2 (87.2–94.1)	28.4 (20.2–38.4)	88.7 (84.2–92.1)		
PPV, % (95 %CI)	31.6 (18.0–48.8)	70.3 (64.1–75.9)	26.2 (14.4–42.3)		
NPV, % (95 %CI)	93.4 (89.7–95.9)	36.3 (26.0–47.8)	85.6 (80.8–89.3)		
Accuracy, % (95 %CI)	86.2 (82.0–89.5)	62.0 (56.6–67.2)	77.9 (73.1–82.3)		

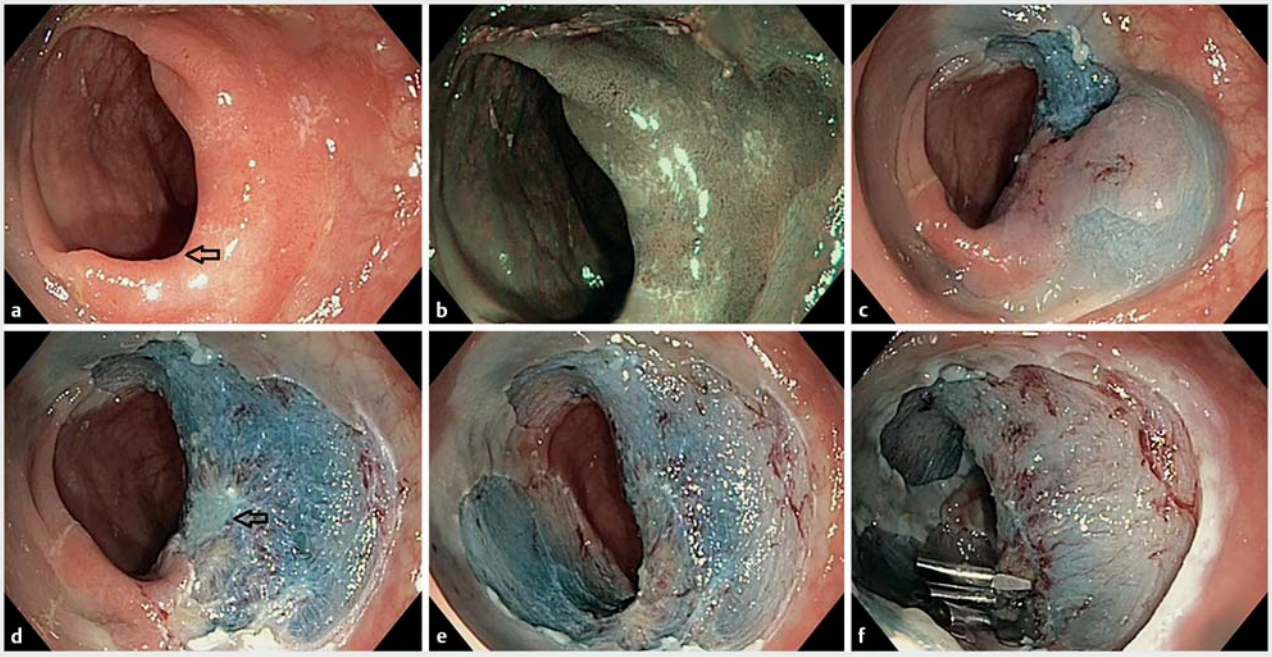
EMR, endoscopic mucosal resection; LGD, low grade dysplasia; HGD, high grade dysplasia; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.
NB: no pre-EMR biopsy showing cancer.
Sensitivity and PPV are with respect to final EMR specimen dysplasia.
Bold type indicates disagreement between biopsy and the final EMR specimen.

histology in 5 % [18]. Such findings are unsurprising given that a superficial biopsy of 1–2 mm in size is unlikely to sample deep within a lesion where more advanced histology may reside.

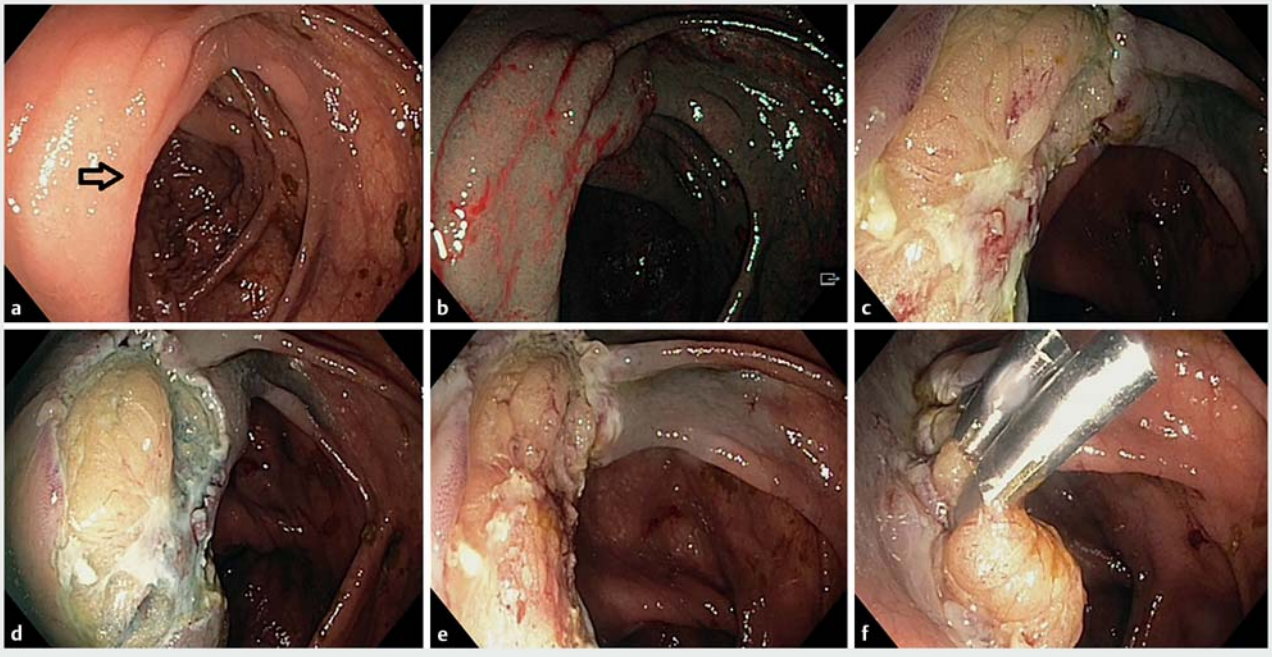
PRB was associated with increased IPB (31.5 % vs. 23.5 %; P = 0.03), but without significant increase in clinically significant post-EMR bleeding, intraprocedural deep mural injury, or delayed perforation. Lesions with PRB, compared with lesions without PRB, had more submucosal fibrosis (43.1 % vs. 30.0 %, respectively; P = 0.001) (▶ **Fig. 3**, ▶ **Fig. 4**) and trended toward longer procedure durations (median duration 25 minutes vs. 20 minutes, respectively; P = 0.06). It is likely that submucosal fibrosis develops following scarring at the site of biopsy, particularly if taken from flat areas. Both IPB and submucosal fibrosis are known risk factors for early recurrence (relative risk 1.68) and failure to perform complete EMR, respectively [7, 16, 19]. Adjunctive resection methods such as cold forceps avulsion followed by snare tip soft coagulation may be required in such situations [16]. Therefore, PRB may result in increased risk and complexity of the EMR procedure.

Given the shortcomings in diagnostic information and possible hazards from PRB, lesion assessment by noncontact modalities is preferable. Assessment of lesion morphology and surface pit and vascular pattern using enhanced endoscopic imaging including NBI and magnifying chromoendoscopy improves identification of submucosal invasion in LNPCPs, which typically reside in depressed areas, with disruption of pit and vascular pattern [2, 5]. For example, predictors of superficial submucosal invasion include surface depression (Paris 0-IIc), nongranularity (NG), and fold convergence. Indeed, the risk of submucosal invasion in a 0-IIa + c NG-LNPCP may be as high as 47 %, whereas lesions at the opposite end of the spectrum (granular 0-IIa LNPCPs) harbor very low risk of submucosal invasion (approximately 1 %) [8, 20]. Studies on NBI and magnifying chromoendoscopy show that Sano IIIA and Kudo pit pattern Vi are predictive of superficial submucosal invasion [2]. Targeted biopsies can be taken from areas within selected LNPCPs where there is suspicion of significant submucosal invasion, particularly if confirmation will result in change of management such as surgical resection.

Limitations apply to this study. First, most data for endoscopic imaging-based lesion diagnosis come from academic centers and may not accurately reflect the experience of the broader endoscopic community. Adoption of these techniques are associated with a learning curve as well as interobserver variability. Therefore, although image-based diagnosis is preferable, it may not be feasible in all settings and by all endoscopists. Second, the location of biopsy from the LNPCP was not specified although intuitively these would be targeted toward the most morphologically abnormal areas or areas with subtle disruption of pit pattern. We expect submucosal fibrosis to be more prevalent in depressed and flat areas than nodular areas after biopsy, but this has not been subjected to systematic study. Similarly, other confounders may exist, such as larger lesion size affecting EMR duration. Third, whether the number



▶ **Fig. 3** Submucosal fibrosis from previous nontargeted biopsy of large nonpedunculated colorectal polyp (LNPCP). Endoscopic mucosal resection (EMR) of 40 mm nongranular, Paris 0-IIb, Kudo III LNPCP in the descending colon. **a** On inspection with white-light endoscopy, a focal indentation in the center of the LNPCP suggestive of previous biopsy site was seen (arrow). **b** There was no disruption of the surface pit pattern on narrow-band imaging. **c** The lesion lifted well. **d** An area of submucosal fibrosis (arrow) was seen over the area of initial concern. **e, f** The EMR was completed and the area of submucosal fibrosis was prophylactically closed using three clips.



▶ **Fig. 4** Submucosal fibrosis from previous nontargeted biopsy of large nonpedunculated colorectal polyp (LNPCP). Endoscopic mucosal resection of 30 mm nongranular, Paris 0-IIa, Kudo III LNPCP over the ileocecal valve. **a** A focal indentation over the center of the LNPCP was the site of previous biopsy (arrow). **b** On narrow-band imaging, the surface pit pattern was not disrupted. **c, d** Piecemeal snare resection revealed an area of central fibrosis resistant to snare capture. **e** This was removed by cold forceps biopsy and snare tip thermal ablation (soft coagulation, 80 W, effect 4). **f** The treated area was prophylactically closed with clips.

of biopsies taken affects submucosal fibrosis and procedural outcomes is unknown. The results from this study were derived from a single referral center and may not necessarily be generalizable to other centers. Finally, given the nature of the study, it was unknown how many lesions assessed by PRB actually had submucosal invasion and thus not referred for EMR.

In conclusion, routine PRB of LNPCPs did not reliably detect advanced dysplastic change, and may provide false reassurance regarding absence of submucosal invasion and lead to submucosal fibrosis with associated increase in EMR complexity. It should therefore be used with caution in selecting lesions suitable for endoscopic resection.

Competing Interests

M. Ma, D. Tate, M. Sidhu, S. Zahid, and M.J. Bourke declare that they have no conflict of interest.M. Ma and D. Tate received a scholarship from the Westmead Medical Research Foundation. These funds were not used for this study. The Cancer Institute New South Wales provided funding for a research nurse and data manager to assist with the administration of the study. There was no influence from the Institution regarding study design or conduct, data collection, management, analysis or interpretation, preparation, review, or approval of the manuscript.

References

[1] Rotondano G, Bianco MA, Buffoli F et al. The Cooperative Italian FLIN Study Group: prevalence and clinico-pathological features of colorectal laterally spreading tumors. Endoscopy 2011; 43: 856–861

[2] Ferlitsch M, Moss A, Hassan C et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2017; 49: 270–297

[3] Ahlenstiel G, Hourigan LF, Brown G et al. Actual endoscopic versus predicted surgical mortality for treatment of advanced mucosal neoplasia of the colon. Gastrointest Endosc 2014; 80: 668–676

[4] Jayanna M, Burgess NG, Singh R et al. Cost analysis of endoscopic mucosal resection vs surgery for large laterally spreading colorectal lesions. Clin Gastroenterol Hepatol 2016; 14: 271–278

[5] Kaltenbach T, Anderson JC, Burke CA et al. Endoscopic removal of colorectal lesions: recommendations by the US Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol 2020; 115: 435–464

[6] Kaminski MF, Hassan C, Bisschops R et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2014; 46: 435–449

[7] Moss A, Williams SJ, Hourigan LF et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut 2015; 64: 57–65

[8] Burgess NG, Hourigan LF, Zanati SA et al. Risk stratification for covert invasive cancer among patients referred for colonic endoscopic mucosal resection: a large multicenter cohort. Gastroenterology 2017; 153: 732–742

[9] Klein A, Bourke MJ. Advanced polypectomy and resection techniques. Gastrointest Endosc Clin N Am 2015; 25: 303–333

[10] Jideh B, Bourke MJ. How to perform wide-field endoscopic mucosal resection and follow-up examinations. Gastrointest Endosc Clin N Am 2019; 29: 629–646

[11] Bourke MJ, Bhandari P. How I remove polyps larger than 20 mm. Gastrointest Endosc 2019; 90: 877–880

[12] Moss A, Bourke MJ, Metz AJ. A randomized, double-blind trial of succinylated gelatin submucosal injection for endoscopic resection of large sessile polyps of the colon. Am J Gastroenterol 2010; 105: 2375–2382

[13] Fahrtash-Bahin F, Holt BA, Jayasekeran V et al. Snare tip soft coagulation achieves effective and safe endoscopic hemostasis during wide-field endoscopic resection of large colonic lesions (with videos). Gastrointest Endosc 2013; 78: 158–163

[14] Burgess NG, Bassan MS, McLeod D et al. Deep mural injury and perforation after colonic endoscopic mucosal resection: a new classification and analysis of risk factors. Gut 2017; 66: 1779–1789

[15] Holt BA, Jayasekeran V, Sonson R et al. Topical submucosal chromoendoscopy defines the level of resection in colonic EMR and may improve procedural safety (with video). Gastrointest Endosc 2013; 77: 949–953

[16] Tate DJ, Bahin FF, Desomer L et al. Cold-forceps avulsion with adjuvant snare-tip soft coagulation (CAST) is an effective and safe strategy for the management of non-lifting large laterally spreading colonic lesions. Endoscopy 2018; 50: 52–62

[17] Klein A, Nayyar D, Bahin FF et al. Endoscopic mucosal resection of large and giant lateral spreading lesions of the duodenum: success, adverse events, and long-term outcomes. Gastrointest Endosc 2016; 84: 688–696

[18] Kakushima N, Ono H, Takao T et al. Method and timing of resection of superficial non-ampullary duodenal epithelial tumors. Dig Endosc 2014; 26: (Suppl. 02): 35–40

[19] Tate DJ, Desomer L, Klein A et al. Adenoma recurrence after piecemeal colonic EMR is predictable: the Sydney EMR recurrence tool. Gastrointest Endosc 2017; 85: 647–656

[20] Moss A, Bourke MJ, Williams SJ et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology 2011; 140: 1909–1918