

## Endoscopic mucosal resection of colorectal polyps in typical UK hospitals

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### Abstract

**AIM:** To evaluate the outcomes of endoscopic mucosal resection (EMR) for colorectal polyps, with particular regard to procedural complications and recurrence rate, in typical United Kingdom (UK) hospitals that perform an average of about 25 colonic EMRs per year.

**METHODS:** A total of 239 colorectal polyps ( $\geq 10$  mm) resected from 199 patients referred to Rochdale Infirmary, Salford Royal Hospital and Royal Oldham Hospital for EMR between January 2003 and January 2009 were studied.

**RESULTS:** The mean size of polyps resected was  $19.6 \pm 12.4$  mm (range 10-80 mm). The overall major complication rate was 2.1%. Complications were less frequent with non-adenomas compared with the other groups (Pearson's  $\chi^2$  test,  $P < 0.0001$ ). Resections of larger-sized polyps were more likely to result in complications (unpaired  $t$ -test,  $P = 0.021$ ). Recurrence was associated with histology, with carcinoma-*in-situ* more likely to recur compared with low-grade dysplasia [hazard ratio (HR) 186.7, 95% confidence interval (95% CI): 8.81-3953.02,  $P = 0.001$ ]. Distal lesions were also more likely to recur compared with right-sided and transverse colon lesions (HR 5.93, 95% CI: 1.35-26.18,  $P = 0.019$ ).

**CONCLUSION:** EMR for colorectal polyps can be performed safely and effectively in typical UK hospitals. Stricter follow-up is required for histologically advanced lesions due to increased recurrence risk.

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**Key words:** Endoscopic mucosal resection; Polyps; Endoscopic; Resection

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### INTRODUCTION

The use of endoscopic mucosal resection (EMR), pio-

neered in Japan for the treatment of early gastric cancer<sup>[1]</sup>, has expanded to include therapy of other early gastrointestinal malignancies and pre-cancerous lesions such as adenomas<sup>[2]</sup> or early stage colon cancers<sup>[3,4]</sup>.

EMR allows the removal of tissue to the level of the muscularis propria and is a good alternative to surgery, thereby eliminating the need for surgical intervention and its associated morbidity and mortality. Early stage colon cancer, adenomas and rectal carcinoid have all been successfully removed by EMR. Resection of polyps can be performed *en bloc* or piecemeal according to the size and location of the lesion. The complication rate associated with EMR is low<sup>[5]</sup>. The most frequent adverse event is bleeding<sup>[6-10]</sup> followed by perforation<sup>[3,11,12]</sup>. Another risk following EMR is recurrence<sup>[8-10,13]</sup>.

The use of EMR for colorectal polyps has become increasingly popular in Western countries and has been found to be a safe and efficient treatment. However, most reports come from large, tertiary referral practices and the applicability to more typical hospitals in the UK has not been established.

This study aims to evaluate the outcomes of EMR for colorectal polyps with particular regard to procedural complications and recurrence rate across three hospitals in North West England which perform an average of about 25 colonic EMR per year.

## MATERIALS AND METHODS

### Study population

All colorectal polyps referred to Rochdale Infirmary, Salford Royal Hospital and Royal Oldham Hospital for EMR between January 2003 and January 2009 were considered for the study. There is one endoscopist performing the EMR procedures in each center. Polyps  $\geq 10$  mm in diameter were selected for the study. Non-lifting lesions or laterally spreading lesions were excluded as these were referred for open surgical resection. Polyps were identified using a detailed record of procedures performed in the endoscopy unit and operating theatres in the three hospitals both for in-patients and out-patients. A total of 239 polyps resected (from 199 patients) were identified for the study.

### Resection method

EMR was performed with a standard polypectomy snare (Olympus SnareMaster SD-230U). The lesion was first lifted by injection of a large volume (10-100 mL) of a pre-mixed solution around the lesion. This consisted of 40 mL Volplex (succinylated gelatine 20 g in 500 mL), 2 mL of 1:10 000 adrenaline, and 2 mL of 0.4% indigo carmine. The open snare was placed around the lesion and was gently pressed against the mucosa. Excess air was aspirated from the colon to decrease distension and facilitate grasping of the targeted polyp. The aim was to resect lesions in one single piece rather than piecemeal if possible. After snare excision, air was insufflated to visualize the area of resection and, if needed, any further residual tissue was removed in similar fashion. Adjutant

argon plasma coagulation (APC) therapy was used to remove tiny remnants of lesions visible after resection. The settings used were "auto-cut" at a fixed power of 120 W, as recommended by the manufacturer, along with the "endo-cut" mode. APC was applied in short bursts to avoid thermal damage to the muscularis propria.

Procedures were performed with the patient under conscious sedation (intravenously administered midazolam and/or pethidine/fentanyl). When required, hyoscine-butyl bromide was given intravenously.

### Assessment of dimension of polyps and histopathology

The size of polyps was estimated by comparison with open biopsy forceps and when possible after retrieval. All removed tissue was retrieved using a Roth net, retrieval basket, grasper or through the suction channel.

All retrieved polyps were examined and classified by experienced pathologists at the respective histopathology departments of each hospital. Polyps were classified as adenoma, carcinoma-*in-situ* (CIS) or non-adenoma (e.g. hyperplastic polyps, lipoma).

Adenomas were further classified according to the Konishi-Morson system for grade of dysplasia (i.e. low-, moderate-, or high-grade) using a combination of variables, including tubule configuration, nuclear polarity, orientation and structure, mucin content and location, *etc.*<sup>[14]</sup>. The diagnosis of CIS included adenomas with neoplastic cells invading into the lamina propria mucosae<sup>[15,16]</sup>.

### Record of complications

Patients were instructed to report symptoms of continuing abdominal pain or bleeding per rectum. The diagnosis of post-procedure bleeding was based on the passage of fresh blood per rectum. Intra-procedural perforation was diagnosed by endoscopy during the resection and confirmed by air on plain abdominal film and/or abdominal computed tomography scan. Post-procedural perforation characterized by abdominal pain and leucocytosis was diagnosed by the presence of free air on plain abdominal film and/or abdominal computed tomography scan.

### Follow-up and recurrence

Surveillance colonoscopy was performed at various intervals, at the discretion of the clinician in charge of the individual patient's care. During endoscopic follow-up, any alterations of the mucosa in the area of previous resection (ulcerations, scarring, retractions of mucosa, *etc.*) were biopsied. Recurrence was defined as the presence of adenomatous or polypoid tissue on a follow-up endoscopy. This was treated with a repeat EMR if possible.

### Statistical analysis

Data are presented as mean  $\pm$  SD and range unless otherwise stated.

Association of complications with different variables was assessed using unpaired *t*-test or Pearson's  $\chi^2$  test. In patients who underwent endoscopic surveillance, the Cox univariate analysis was used to identify significant prognostic factors. *P* values  $< 0.05$  were regarded as statistically

**Table 1 Patient demographics *n* (%)**

	No. of patients ( <i>n</i> = 199)
Age (yr) <sup>1</sup>	68.0 ± 11.4
Sex	
M	119 (59.8)
F	80 (40.2)
Polyp location	
Cecum	49 (20.5)
Ascending colon	30 (12.6)
Transverse colon	26 (10.9)
Descending colon	34 (14.2)
Sigmoid colon	43 (18.0)
Rectum	57 (23.8)
Total	239
Polyp size (mm) <sup>1</sup>	68.0 ± 11.4
Range (mm)	10-80

<sup>1</sup>Values are mean ± SD. Values are number of patients with percentages in parentheses unless indicated otherwise.

**Table 2 Characteristics of polyps according to histopathology *n* (%)**

	Non-adenomas	Adenomas	Carcinoma- <i>in-situ</i>
Age (yr) <sup>1</sup>	61.3 ± 12.9	69.2 ± 9.9	76.2 ± 11.2
Sex			
M	15	117	9
F	23	64	4
Polyp size (mm) <sup>1</sup>	13.9 ± 5.2	20.8 ± 13.1	22.7 ± 14.9
Polyp location			
Cecum	13 (34.2)	31 (17.1)	2 (15.4)
Ascending colon	5 (13.2)	24 (13.3)	0
Transverse colon	9 (23.7)	15 (8.3)	1 (7.7)
Descending colon	4 (10.5)	29 (16.0)	0
Sigmoid colon	6 (15.8)	33 (18.2)	3 (2.3)
Rectum	1 (2.6)	49 (27.1)	7 (5.4)
Total	38	181	13
Resection method			
<i>En bloc</i>	33 (86.8)	129 (71.3)	9 (69.2)
Piecemeal	5 (13.2)	50 (27.6)	4 (30.8)
Not recorded	0	2 (1.1)	0
Complete resection			
Yes	36 (94.7)	154 (85.1)	10 (76.9)
No	2 (5.3)	26 (14.4)	3 (23.1)
Not recorded	0	1 (0.5)	0
Recurrence <sup>2</sup>			
No		75 (48.8)	1 (10.0)
Yes		30 (19.4)	3 (30.0)
No follow up		49 (31.8)	6 (60.0)

<sup>1</sup>Values are mean ± SD; <sup>2</sup>Only completely resected lesions were assessed for recurrence. Values are number of patients with percentages in parentheses unless indicated otherwise.

significant. Statistical analysis was performed using SPSS 15.0 statistical package (SPSS Inc., Chicago, IL, USA).

## RESULTS

A total of 239 polyps were treated in 199 patients. Thirty-three patients had more than one polyp. The characteristics of the patient population, and polyp size and location, are presented in Table 1. The mean age of the patients

**Table 3 Hazard ratio for risk of recurrence associated with clinical variables (*n* = 164)**

	Hazard ratio	95% CI	<i>P</i> <sup>1</sup>
Age	1.036	0.982-1.093	0.194
Sex	0.851	0.301-2.403	0.761
Size	1.023	0.974-1.074	0.357
Resection method ( <i>en bloc</i> vs piecemeal)	0.680	0.188-2.452	0.555
Histology			0.004
MGD vs LGD	2.837	0.358-22.499	0.324
HGD vs LGD	2.009	0.206-19.630	0.549
CIS vs LGD	186.651	8.813-3953.020	0.001
Site (distal colon vs right and transverse colon)	5.933	1.345-26.175	0.019

<sup>1</sup>Cox univariate analysis. LGD: Low-grade dysplasia; MGD: Moderate-grade dysplasia; HGD: High-grade dysplasia; CIS: Carcinoma-*in-situ*.

was 68.0 ± 11.4 years and approximately 60% of the patients were male. The mean size of polyps resected was 19.6 ± 12.4 mm (range 10-80 mm).

A breakdown of polyps resected according to histopathology is shown in Table 2. Of the adenomas resected, 47 (26.0%) polyps were classified as low-grade dysplasia (LGD), 77 (42.5%) moderate-grade dysplasia (MGD), 49 (27.1%) high-grade dysplasia (HGD), and the classifications of eight polyps were unrecorded.

Complete resection was achieved in 86.2%. Patients who failed to have polyps completely resected were either referred for surgery or had their polyps resected in a repeat session. These patients were excluded from surveillance analysis (see below).

## Complications

Two patients had significant post-procedural bleeding. One patient responded to intravenous fluid resuscitation and blood transfusion, while the other required a sigmoid colectomy to treat the bleeding. Two patients developed post-procedural perforation. One patient was managed conservatively; while the other went on to have surgery (anterior resection of rectum). No procedure-related mortality was reported. The overall major complication rate was 2.1%.

Complications were less frequent with non-adenomas compared with the other groups (Pearson's  $\chi^2$  test, *P* < 0.0001). Resections of larger-sized polyps were more likely to result in complications (unpaired *t*-test, *P* = 0.021).

## Surveillance

Seventy-eight out of 139 patients (164 polyps) with completely resected adenomas and CIS underwent follow-up colonoscopy (56.1%). Median follow up was 6.8 mo (range 1.2-26.6 mo).

Local recurrence was detected at 33 resection sites. The histopathology of the recurrent polyps was as follows: 7 (21.2%) LGD, 16 (48.5%) MGD, 7 (21.2%) HGD, and 3 (9.1%) CIS.

On univariate analysis (Table 3), recurrence was associated with histology, with CIS more likely to recur compared with LGD [hazard ratio (HR) 186.7, 95% con-

fidence interval (95% CI): 8.81-3953.02,  $P = 0.001$ ]. Distal lesions were also more likely to recur compared with right-sided and transverse colon lesions (HR 5.93, 95% CI: 1.35-26.18,  $P = 0.019$ ).

## DISCUSSION

Several studies have been published regarding the safety and therapeutic potential of endoscopic resection of colorectal polyps. The most frequent adverse event of EMR reported is bleeding, occurring in 1% to 45% of cases<sup>[6-10]</sup>. Perforation rate has been reported to be between 0.7% and 4%<sup>[3,11,12]</sup>. The overall serious complication rate in the present study is only 2.1%, although one of the main drawbacks of the study is the lack of data on intra-procedural bleeding. However, this is often self-limiting or can be treated successfully during the procedure. Complication rates of EMR are lower than those of open surgery (2.3% to 6.3%) and comparable to those of laparoscopic surgery (1.9% to 6.9%)<sup>[17]</sup>. However, mean hospital stay for the patients who undergo colorectal surgery is 9.2-13.2 d, significantly longer than for patients who undergo EMR procedures, which are usually performed as day cases<sup>[17]</sup>. Therefore, EMR is a good alternative to surgery in a selected group of patients unfit for surgery.

The present study highlights that increasing size of polyp resected is associated with complications and the authors recommend that extra care should be taken in resecting polyps of > 35 mm in diameter.

Where possible all lesions were removed in a single session as this eliminates the discomfort and the inconvenience of repeated procedures for patients. This was achieved in 86.2% of resections in the present study. Preference has been suggested in some studies for *en bloc* resection compared with piecemeal resection, because it provides more accurate histological assessment and reduces the risk of local recurrence<sup>[18]</sup>. However, in the present study there was no statistically significant difference in the recurrence rate reported between the two resection techniques.

Follow-up is essential because of the risk of recurrence. Aggressive surveillance seems justified because it has been shown, in an animal model, that residual tumor has a high regrowth rate<sup>[19]</sup>. Unfortunately, only about half of the patients in the present study underwent a follow-up colonoscopy. The main reasons for non follow-up were patient refusal and patient frailty.

Recurrence rates after EMR of colorectal polyps have been reported to be between 0% and 46%<sup>[8-10,13]</sup>. In the present study, the recurrence rates were 19.5% for non-malignant polyps and 30% for malignant polyps. Several studies have suggested that size of polyps is associated with recurrence. However, this was not found in the present study. Instead, recurrence was more common in distal and/or more histologically advanced lesions.

The present study has shown that EMR for colorectal polyps can be carried out safely and effectively in typical UK hospitals provided the endoscopists carrying out the procedures have the appropriate training and in-

terest in EMR. This procedure should be considered in preference to open surgery, especially in polyps smaller than 35 mm in diameter. Also, a stricter follow-up may be required for more histologically advanced lesions because of a higher risk of recurrence.

## COMMENTS

### Background

The use of endoscopic mucosal resection has expanded to include therapy of early gastrointestinal malignancies and pre-cancerous lesions such as adenomas or early stage colon cancers, especially in Western countries. However, most studies have come from large tertiary centers in the world.

### Research frontiers

In this study, the authors demonstrate that endoscopic mucosal resection of colorectal polyps can be performed safely and effectively in typical United Kingdom (UK) hospitals, with complication rates and recurrence rates which are comparable to tertiary centers.

### Innovations and breakthroughs

This is the first study to report results from the practice of endoscopic mucosal resection of colorectal polyps in typical UK hospitals where an endoscopist performs an average of 25 of these procedures per year.

### Applications

It can be established from this study that patients from non-tertiary centres which have similar experience in endoscopic mucosal resection may be reassured that the procedures can be performed safely and effectively.

### Terminology

Endoscopic mucosal resection allows the removal of tissue to the level of the muscularis propria and is a good alternative to surgery, thereby eliminating the need for surgical intervention and its associated morbidity and mortality.

### Peer review

The take home message from this study is that it is feasible to perform endoscopic mucosal resection in a community hospital with a trained endoscopist.

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