RESEARCH ARTICLE

Management of malignant T1 colorectal cancer polyps: results from a 10-year prospective observational study

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Abstract

Aim: The recurrence risk associated with residual malignant cells (bowel wall/regional nodes) following T1 colorectal cancer (CRC) polypectomy must be weighed against operative morbidity. Our aim was to describe the management and outcomes of a large prospective cohort of T1 CRCs.

Method: All T1 CRCs diagnosed between March 2007 and March 2017 at the Glasgow Royal Infirmary were included. Patients were grouped by polypectomy, rectal local excision and formal resection status. χ^2 testing, multivariate binary logistic and Cox regression were performed.

Results: Of 236 patients, 90 (38.1%) underwent polypectomy only, six (2.6%) polypectomy and then rectal excision, 57 (24.2%) polypectomy and then resection, 14 (5.9%) rectal excision only and 69 (29.2%) primary resection. Polypectomy only correlated with male sex ($P=0.028$), older age ($P<0.001$), distal CRCs ($P<0.001$) and pedunculated polyps ($P<0.001$); primary resection with larger polyps ($P<0.001$); polypectomy then resection with piecemeal excision ($P=0.002$) and involved polypectomy margin ($P<0.001$). Poor differentiation (OR 7.860, 95% CI 1.117–55.328; $P=0.038$) independently predicted lymph node involvement. Submucosal venous invasion (hazard ratio [HR] 10.154, 95% CI 2.087–49.396; $P=0.004$) and mucinous subtype (HR 7.779, 95% CI 1.566–38.625; $P=0.012$) independently predicted recurrence. Submucosal venous invasion (HR 5.792, 95% CI 1.056–31.754; $P=0.043$) predicted CRC-specific survival. Although 64.4% of polypectomy-only patients had margin involvement/other risk factors, none developed recurrence. Of 94 with polypectomy margin involvement, five (5.3%) had confirmed residual tumour. Overall, lymph node metastases (7.1%), recurrence (4.2%) and cancer-specific mortality (3.0%) were rare. Cancer-specific 5-year survival was high: polypectomy only (100%), polypectomy and then resection (98.2%), primary resection (100%).

Conclusion: Surveillance may be safe for more T1 CRC polyp patients. Multidisciplinary team discussion and informed patient choice are critical.

KEYWORDS
cancer, colorectal, polyps, T1

INTRODUCTION

Colorectal cancer (CRC) is the fourth most common cancer in the UK, with approximately 43 000 new cases and 17 000 deaths each year [1]. CRCs originate from premalignant polyps, both adenomas and less commonly sessile serrated polyps [2–5]. With the introduction of the Bowel Screening Programme there has been an increase in the number of early-stage CRCs diagnosed and a resultant decrease in cancer-specific mortality [6]. A malignant polyp is one which contains adenocarcinoma with evidence of invasion through the muscularis mucosae and into but not beyond the submucosa (T1 staged) [7, 8]. These account for 10% of all screen-detected CRCs [6]. Advancing endoscopic technology means an increasing number of malignant polyps are resected at colonoscopy [8, 9]. This has created a management dilemma: the recurrence risk associated with leaving residual malignant cells within the bowel wall or regional lymph nodes must be weighed against the morbidity associated with progressing to formal colorectal resection [8].

To date, the evidence on which our practice is based is limited, retrospective and heterogeneous and no randomized control trials exist. Overall, malignant polyps are associated with a low risk of lymph node metastasis, disease recurrence and cancer-specific mortality [8, 9]. Therefore, large studies are required to predict associated risk factors. The most widely reported risk factors include submucosal venous invasion (SMVI), submucosal lymphatic invasion (SMLI) [8, 10, 11], poor differentiation [8, 12, 13], positive endoscopic polypectomy resection margin (≤1 mm clearance from malignant cells) [8, 10, 14] and mucinous-subtype CRCs [15]. Others include submucosal tumour depth >1000 µm [11], the presence of tumour budding [11, 16], Haggitt level 4 [8, 17] and Kikuchi level SM3 [8, 18]. Notably, even with the presence of high risk features, the chance of residual cancer being found at the polypectomy resection site or in locoregional lymph nodes at formal resection is low [19]. Therefore, it is important to thoroughly discuss operative morbidity, the possibility of a permanent stoma and sexual/urinary dysfunction even where high risk features are present, to ensure an informed decision is made.

While large retrospective studies have identified risk factors associated with an increased risk of lymph node metastases or disease recurrence, there is a distinct paucity of prospective data. The aim of the current study was therefore to describe the management and outcome of patients with T1 polyp CRCs in a large, tertiary teaching hospital, collected over a 10-year period, and validate previously identified risk factors for lymph node metastases, recurrence and cancer-specific survival (CSS) in this prospective cohort.

METHODS

Study design, setting and participants

A prospective observational study was conducted. All patients diagnosed with T1 CRC between March 2007 and March 2017 at the Glasgow Royal Infirmary were prospectively entered into the study,

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What does this paper add to the literature?

Few prospective T1 polyp colorectal cancer studies exist with long-term follow-up. Novel findings of this study include 0% recurrence in polypectomy-alone patients despite most having ≥1 recognized risk factor and only 5% with positive polypectomy margin having evidence of residual cancer. Endoscopic surveillance may be considered for such patients.

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with the finalized histopathological staging used to define T1 tumours. Patients were identified from the local cancer registry to ensure no missed cases. Caldicott Guardian approval was given by National Health Service (NHS) Greater Glasgow and Clyde to safeguard the data with ethical approval waived for the purposes of service development and results reported according to STROBE guidelines [20]. As this was a purely observational study with no impact on patient management, individual consent was not obtained from each patient.

Variables and data sources

To obtain patient demographics and outcomes cross-referencing of the NHS Clinical Portal was performed with the community health index number used as the linkage variable. This allowed access to clinic letters, colonoscopy reports, operation notes and pathology records. Variables collected included age at time of primary procedure, sex, tumour location, polyp morphology (pedunculated or sessile), whether polypectomy was performed, whether this was whole or piecemeal and whether a definitive procedure was performed (formal colorectal resection or rectal local excision). The presence of recognized risk factors for residual disease or recurrence was documented: SMVI, SMLI, poor differentiation, mucinous subtype, submucosal depth >1000 µm, Haggitt level, Kikuchi level and a positive endoscopic resection margin (≤1 mm clearance from malignant cells). Outcomes recorded were the presence of lymph node involvement (where a formal resection was performed), disease recurrence and cancer-specific mortality.

Data analysis and statistical methods

For the purposes of analysis patients were divided firstly by whether polypectomy was performed and secondly by method of definitive management: no further procedure, rectal local excision (trans-anal endoscopic microsurgery, trans-anal minimally invasive surgery or trans-anal excision) or formal colorectal resection. This produced five treatment groups for comparison. Covariables were compared using crosstabulation and the χ^2 test for linear trend. A value of $P<0.05$ was considered statistically significant. To identify variables which independently predicted lymph node metastases binary logistic regression was performed, allowing calculation of ORs and 95% CIs. To identify variables which independently predicted

disease recurrence and CSS, Cox regression analysis was used with resultant hazard ratios (HRs) and 95% CIs presented. In all cases, covariables $P<0.1$ on univariate analysis were entered into a multivariate model using the backwards conditional method in which variables with a significance of $P>0.1$ were removed from the model in a stepwise fashion. Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA).

RESULTS

Participants and outcomes

Between March 2007 and March 2017, 236 patients were diagnosed with a T1 CRC at the Glasgow Royal Infirmary. Five patients had two synchronous T1 CRCs and one patient had three. Median age was 68 years (interquartile range [IQR] 61–75) and 103 (43.6%) were women. 113 (47.9%) were screen-detected whilst 123 (52.1%) were diagnosed via symptomatic or surveillance pathways. Figure 1 shows the management pathway of all patients, including division into our five predefined management groups. A comparison of demographics, pathology and outcomes between the groups can be seen in Table 1. Overall, nine of 126 (7.1%) patients who underwent resection had lymph node involvement. With a median follow-up of 7.4 years (IQR 5.0–9.9 years), 10 of 236 (4.2%) patients developed recurrent disease and seven (3.0%) died of CRC.

Group I—Polypectomy only

Ninety patients were managed with polypectomy only. 38 of 90 (42.2%) had ≥1 risk factor excluding a positive polypectomy resection margin and 58 (64.4%) had ≥1 risk factor of any type. The reasons for not proceeding to resection in these 58 patients were that 32 (55.2%) were unfit for resection, nine (15.5%) followed a multidisciplinary team (MDT) decision, six (10.3%) were patient choice, two underwent chemoradiotherapy and one radiotherapy instead to avoid abdominoperineal resection of the rectum and eight (13.8%) were unclear. Of 38 patients with an involved polypectomy resection margin, 31 (81.6%) had a colonoscopy/sigmoidoscopy site check within 6 months. Long-term follow-up varied but most had a colonoscopy, CT and clinic review. With a median follow-up of 7.2 years, no patients developed recurrent disease or died of CRC with a 5-year CSS of 100%.

Group II—Polypectomy followed by excision of rectal scar

Six patients proceeded from rectal polypectomy to local rectal excision. All six polyps were sessile. All six had a positive polypectomy resection margin. Three had additional risk factors. With a median follow-up of 6.0 years, no patients developed recurrent disease or died of CRC. Five-year CSS was 100%.

Group III—Polypectomy followed by formal colorectal resection

Fifty-seven patients proceeded from polypectomy to formal surgical resection. 25 of 57 (43.9%) patients had ≥1 risk factor excluding a positive polypectomy margin and 55 (96.5%) had ≥1 risk factor of any type. Following pathological examination, five of 57 (9%) resection specimens were found to have residual disease: one (1.8%) small focus at the polypectomy site, one (1.8%) case of extramural venous invasion and three (5.3%) patients had lymph node involvement. All five had an involved polypectomy margin and three had another risk factor. With a median follow-up of 7.7 years, four (7.0%) patients developed disseminated metastatic disease. None of these four patients had residual tumour in their resection specimens, including no nodal disease. The median
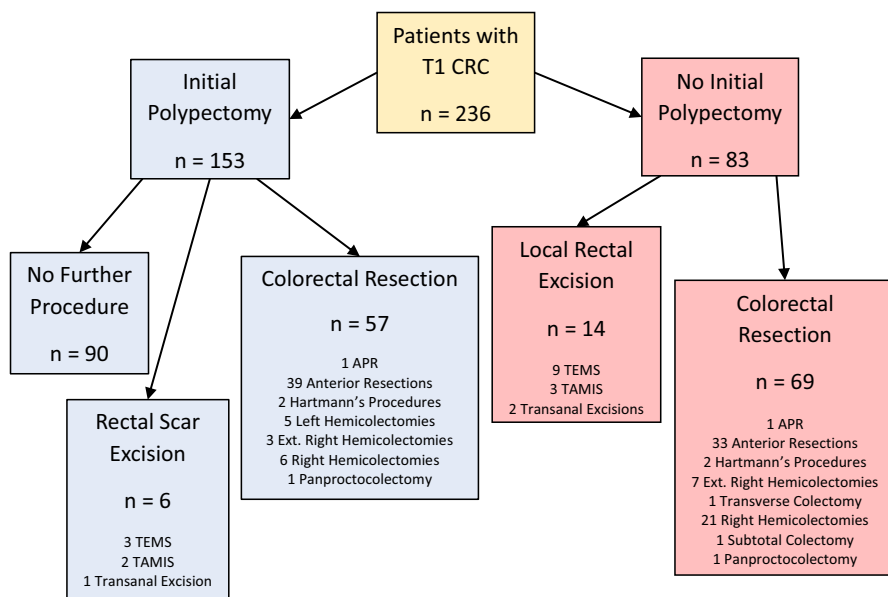
FIGURE 1 Management pathway of all 236 patients with T1 colorectal cancer.

TABLE 1 Comparison of demographics, pathological characteristics and recognized risk factors for residual/recurrent disease between all five treatment groups.

	All	Group I: Polypectomy only	Group II: Excision of rectal scar after polypectomy	Group III: Polypectomy then colorectal resection	Group IV: Rectal excision only	Group V: Colorectal resection only	P (group I vs. group III vs. group V comparison)
Total	236	90	6	57	14	69	
Sex							
Male	133 (56%)	60 (67%)	4 (67%)	28 (49%)	8 (57%)	33 (48%)	0.023
Female	103 (44%)	30 (33%)	2 (33%)	29 (51%)	6 (43%)	36 (52%)	
Age (years), median (range)	68 (27–93)	71 (46–93)	65 (57–88)	63 (27–79)	73 (56–80)	69 (32–83)	<0.001
Location							
Colonic	163 (69%)	67 (74%)	0 (0%)	44 (77%)	0 (0%)	52 (75%)	<0.001
Rectal	73 (31%)	23 (26%)	6 (100%)	13 (23%)	14 (100%)	17 (25%)	
Diagnosis							
Screen detected	113 (48%)	45 (50%)	4 (67%)	29 (50%)	5 (36%)	30 (44%)	0.639
Symptomatic	123 (52%)	45 (50%)	2 (33%)	28 (49%)	9 (64%)	39 (57%)	
Morphology							
Pedunculated	70 (30%)	45 (50%)	0 (0%)	16 (28%)	1 (7%)	8 (12%)	<0.001
Sessile	166 (70%)	45 (50%)	6 (100%)	41 (72%)	13 (93%)	61 (88%)	
Polypectomy							
Whole	115 (75%)	76 (84%)	4 (67%)	35 (61%)	NA	NA	0.002
Piecemeal	38 (25%)	14 (16%)	2 (33%)	22 (39%)	NA	NA	
Polyp size (mm), median (range)	20 (5–75)	16 (5–42)	14 (8–21)	17 (5–50)	35 (20–70)	25 (5–75)	<0.001
SMVI							
Present	57 (24%)	13 (14%)	3 (50%)	11 (19%)	8 (57%)	22 (32%)	0.124
Absent	149 (63%)	61 (68%)	3 (50%)	34 (60%)	5 (36%)	46 (67%)	
Not reported	30 (13%)	16 (18%)	0 (0%)	12 (21%)	1 (7%)	1 (1%)	
SMLI							
Present	23 (12%)	10 (11%)	0 (0%)	6 (11%)	3 (21%)	4 (6%)	0.305
Absent	169 (72%)	63 (70%)	6 (100%)	33 (58%)	10 (71%)	57 (83%)	
Not reported	44 (19%)	17 (19%)	0 (0%)	18 (32%)	1 (7%)	8 (12%)	
Differentiation							
Poor	10 (4%)	3 (3%)	0 (0%)	4 (7%)	0 (0%)	3 (4%)	0.561
Moderate	186 (79%)	70 (78%)	6 (100%)	46 (81%)	10 (71%)	54 (78%)	
Well	20 (9%)	7 (8%)	0 (0%)	1 (2%)	2 (14%)	10 (15%)	
Not reported	20 (9%)	10 (11%)	0 (0%)	6 (11%)	2 (14%)	2 (3%)	

TABLE 1 (Continued)

	All	Group I: Polypectomy only	Group II: Excision of rectal scar after polypectomy	Group III: Polypectomy then colorectal resection	Group IV: Rectal excision only	Group V: Colorectal resection only	P (group I vs. group III vs. group V comparison)
Mucinous							
Yes	11 (%)	4 (4%)	0 (0%)	2 (4%)	1 (7%)	4 (6%)	0.826
No	225 (95%)	86 (96%)	6 (100%)	55 (97%)	13 (93%)	65 (94%)	
Submucosal depth							
>1 mm	24 (10%)	13 (14%)	0 (0%)	7 (12%)	3 (21%)	1 (1%)	NA
≤1 mm	9 (4%)	5 (6%)	0 (0%)	0 (0%)	2 (14%)	2 (3%)	
Not reported	203 (86%)	72 (80%)	6 (100%)	50 (88%)	9 (64%)	66 (96%)	
Haggitt level							
4	4 (2%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	3 (4%)	NA
3	14 (6%)	4 (4%)	0 (0%)	7 (12%)	1 (7%)	2 (3%)	
2	12 (5%)	7 (8%)	0 (0%)	4 (7%)	0 (0%)	1 (1%)	
1	9 (4%)	6 (7%)	0 (0%)	0 (0%)	0 (0%)	3 (4%)	
Not reported	197 (84%)	72 (80%)	6 (100%)	46 (81%)	13 (93%)	60 (87%)	
Kikuchi level							
3	14 (6%)	0 (0%)	0 (0%)	4 (7%)	4 (29%)	6 (9%)	NA
2	8 (3%)	1 (1%)	0 (0%)	2 (4%)	4 (29%)	2 (3%)	
1	8 (3%)	4 (4%)	1 (17%)	0 (0%)	2 (14%)	1 (1%)	
Not reported	206 (87%)	85 (94%)	5 (83%)	51 (90%)	4 (29%)	60 (87%)	
Margin							
≤1 mm	94 (61%)	38 (42%)	6 (100%)	50 (88%)	NA	NA	<0.001
>1 mm	59 (39%)	52 (58%)	0 (0%)	7 (12%)	NA	NA	
≥1 risk factor excl. margin involvement	111 (47%)	38 (42%)	3 (50%)	25 (44%)	12 (86%)	33 (48%)	NA
≥1 risk factor incl. margin involvement	164 (69%)	58 (64%)	6 (100%)	55 (97%)	NA	NA	NA
Residual disease at polypectomy site	1 (0.5%)	NA	0 (0%)	1 (2%)	NA	NA	NA
EMVI	2 (1%)	NA	NA	1 (2%)	NA	1 (1%)	NA
Lymph node involvement	9 (4%)	NA	NA	3 (5%)	NA	6 (9%)	NA

TABLE 1 (Continued)

	All	Group I: Polypectomy only	Group II: Excision of rectal scar after polypectomy	Group III: Polypectomy then colorectal resection	Group IV: Rectal excision only	Group V: Colorectal resection only	P (group I vs. group III vs. group V comparison)
Median follow-up (years)	7.2	7.2	6.0	7.7	6.7	7.6	NA
Recurrence	10 (4%)	0 (0%)	0 (0%)	4 (7%)	3 (21%)	3 (4%)	NA
CRC death	7 (3%)	0 (0%)	0 (0%)	4 (7%)	1 (7%)	2 (3%)	NA

Abbreviations: CRC, colorectal cancer; EMVI, extramural venous invasion; SMLI, submucosal lymphatic invasion; SMVI, submucosal venous invasion.

survival of these four patients was 7.9 years and only one patient died before 5 years with a 5-year CSS for this group of 98.2%.

Group IV—Rectal excision only

Fourteen patients underwent rectal local excision alone. Twelve (85.7%) had ≥1 risk factor. One patient received chemoradiotherapy and two radiotherapy alone. With a median follow-up of 6.7 years, three (21.4%) developed recurrent disease. One patient died at 6 years, one was lost to follow-up at 3.5 years and the final patient is alive at 10 years. Five-year CSS for this group was 98.2%.

Group V—Formal colorectal resection only

Sixty-nine patients proceeded directly to formal colorectal resection. 33 of 69 (47.8%) had ≥1 risk factor. The reasons for no initial polypectomy in these patients were as follows: 20 had lesions too large for endoscopic excision (≥30 mm), seven lesions would not raise on submucosal injection, four had other technical reasons making complete endoscopic resection impossible (excessive looping, lesion on a poorly accessible fold, incomplete colonoscopy but large polyp found on CT colon), three patients declined attempted endoscopic/local resection, five patients were over-staged by imaging (MRI or endoanal ultrasound), seven had other reasons for resection (polyposis, inflammatory bowel disease, colovesical fistula), 14 had resection based on MDT recommendation and eight were unknown. With a median follow-up of 7.6 years, three (4.3%) patients developed recurrent disease and two (2.9%) died from recurrent CRC, both after 5 years, with a 5-year CSS of 100%.

Group comparisons

A formal comparison was made between the three main groups: polypectomy only (group I), polypectomy followed by formal colorectal resection (group III) and formal colorectal resection only (group V; Table 1). A significantly higher proportion of men belonged to the polypectomy-only group (men: group I 66.7%, III 49.1%, V 47.8%; $P = 0.028$). Patients who underwent polypectomy only tended to be older and patients who proceeded from polypectomy to formal colorectal resection younger (median age: group I 71 years, III 63 years, V 69 years; $P < 0.001$). Patients who proceeded directly to formal colorectal resection had a higher proportion of proximal lesions (group I 7.8%, III 26.3%, V 46.4%; $P < 0.001$). Pedunculated polyps represented a higher proportion of those undergoing polypectomy only (group I 50.0%, III 28.1%, V 11.6%; $P < 0.001$). A lower proportion of polypectomies were completed piecemeal in the polypectomy-only group compared to polypectomies performed prior to formal resection (piecemeal polypectomy: group I 15.6%, III 38.6%; $P = 0.002$). Patients who proceeded directly to formal colorectal resection had larger polyps (median polyp size: group I 16 mm, III 17 mm, V 25 mm; $P < 0.001$). In terms of recognized risk factors, there was no significant difference between the groups in SMVI ($P = 0.124$),

SMLI (*P*=0.305), poor differentiation (*P*=0.561) or mucinous subtype (*P*=0.826). Patients who proceeded from polypectomy to formal colorectal resection were more likely to have an involved polypectomy resection margin (group I 42.2%, III 87.7%; *P*<0.001). Of note, for submucosal depth >1000 μm, Haggitt and Kikuchi levels were underreported; these were not included in the formal comparison.

Lymph node metastases—binary logistic regression

On univariate analysis only poor differentiation significantly predicted lymph node metastases (OR 7.000, 95% CI 1.118–43.840; *P*=0.038; Table 2). Polyp size ≥20 mm did not reach significance but as *P*<0.1 it was carried forward to multivariate analysis. On multivariate analysis only poor differentiation independently predicted lymph node metastases (OR 7.86, 95% CI 1.117–55.328; *P*=0.038).

Disease recurrence—Cox regression

On univariate analysis SMVI predicted time to disease recurrence (HR 9.570, 95% CI 1.986–46.113; *P*=0.005) as did mucinous subtype (HR 5.611, 95% CI 1.189–26.471; *P*=0.029; Table 3). On multivariate analysis SMVI (HR 10.154, 95% CI 2.087–49.396; *P*=0.004; Figure 2) and mucinous subtype (HR 7.779, 95% CI 1.566–38.625; *P*=0.012; Figure 3) retained significance as independent predictors of time to disease recurrence.

Cancer-specific survival—Cox regression

On univariate analysis SMVI predicted CSS (HR 5.792, 95% CI 1.056–31.754; *P*=0.043; Table 4; Figure 4). As no other factors were predictive, multivariate analysis was not performed.

TABLE 2 Binary logistic regression analysis of factors associated with risk of lymph node metastases.

	Lymph node metastases		Univariate			Multivariate		
	No	Yes	OR	95% CI	*P*	OR	95% CI	*P*
Sex								
Male	55 (90%)	6 (10%)	1.0	0.106–1.858	0.266			
Female	62 (95%)	3 (5%)	0.444					
Age (years)								
Median (range)	67 (27–83)	67 (32–79)	0.974	0.917–1.034	0.384			
Location								
Colonic	90 (94%)	6 (6%)	1.0	0.391–7.113	0.490			
Rectal	27 (90%)	3 (10%)	1.667					
Morphology								
Pedunculated	23 (96%)	1 (4%)	1.0	0.233–16.443	0.536			
Sessile	94 (92%)	8 (8%)	1.957					
Polyp size								
<20 mm	54 (98%)	1 (2%)	1.0	0.831–56.582	0.074	1.0	0.741–57.055	0.091
≥20 mm	63 (89%)	8 (11%)	6.857			6.502		
SMVI								
No	77 (96%)	3 (4%)	1.0	0.746–16.791	0.111			
Yes	29 (88%)	4 (12%)	3.540					
SMLI								
No	83 (92%)	7 (8%)	1.0	–	0.999			
Yes	10 (100%)	0 (0%)	–					
Poor differentiation								
No	105 (95%)	6 (5%)	1.0	1.118–43.84	0.038	1.0	1.117–55.328	0.038
Yes	5 (71%)	2 (29%)	7.000			7.860		
Mucinous								
No	111 (93%)	9 (8%)	1.0	–	0.999			
Yes	6 (100%)	0 (0%)	–					

Abbreviations: SMLI, submucosal lymphatic invasion; SMVI, submucosal venous invasion.

TABLE 3 Cox regression analysis of factors associated with time to disease recurrence.

|	Recurrence		Univariate			Multivariate		
	No	Yes	HR	95% CI	P	HR	95% CI	P
Sex								
Male	128 (96%)	5 (4%)	1.0	0.358–4.272	0.738			
Female	98 (95%)	5 (5%)	1.236					
Age (years)								
Median (range)	68 (27–93)	67 (52–78)	1.005	0.945–1.069	0.882			
Location								
Colonic	158 (97%)	5 (3%)	1.0	0.671–8.001	0.184			
Rectal	68 (93%)	5 (7%)	2.316					
Morphology								
Pedunculated	68 (97%)	2 (3%)	1.0	0.363–8.060	0.497			
Sessile	158 (95%)	8 (5%)	1.711					
Polyp size								
<20 mm	113 (98%)	2 (2%)	1.0	0.831–18.422	0.084	1.0	0.611–14.494	0.177
≥20 mm	113 (93%)	8 (7%)	3.912			2.976		
SMVI								
No	147 (99%)	2 (1%)	1.0	1.986–46.113	0.005	1.0	2.087–49.396	0.004
Yes	50 (88%)	7 (12%)	9.570			10.154		
SMLI								
No	161 (95%)	8 (5%)	1.0	0.125–7.990	0.999			
Yes	22 (96%)	1 (4%)	0.998					
Poor differentiation								
No	196 (95%)	10 (5%)	1.0	–	0.633			
Yes	10 (100%)	0 (0%)	–					
Mucinous								
No	217 (96%)	8 (4%)	1.0	1.189–26.471	0.029	1.0	1.566–38.625	0.012
Yes	9 (82%)	2 (18%)	5.611			7.779		
Margin ≤1 mm								
No	59 (100%)	0 (0%)	1.0	–	0.373			
Yes	90 (96%)	4 (4%)	–					
Excision								
Local	107 (97%)	3 (3%)	1.0	0.495–7.407	0.347			
Resection	119 (94%)	7 (6%)	1.915					

Abbreviations: HR, hazard ratio; SMLI, submucosal lymphatic invasion; SMVI, submucosal venous invasion.

DISCUSSION

This study describes the management and outcomes of 236 T1 CRC patients prospectively compiled over 10 years. Management varied, with 38.1% having polypectomy alone, 2.5% proceeding from polypectomy to rectal scar excision, 24.2% polypectomy followed by formal colorectal resection and 5.9% and 35.2% local rectal excision or segmental resection respectively as first-line treatment, following lesion biopsy. Overall, outcomes were excellent with low rates of lymph node involvement (7.1%), disease recurrence (4.2%) and cancer-related mortality (3.0%). CSS was 98.3% overall at 5 years and 92.1% at 10 years.

There are a number of histopathological risk factors recognized to be associated with increased likelihood of locoregional lymph node involvement and recurrence in T1 CRCs, including intramural lymphovascular invasion [8, 10, 11], poor differentiation [8, 12, 13] and invasive characteristics such as depth of tumour within the submucosa defined using the Haggit [8, 17] or Kikuchi [8, 18] systems dependent on lesion morphology. In addition, technical factors such as the presence of viable tumour at the lateral or deep excision margins have been reported to be associated with local recurrence [8, 10]. In the current, prospective study, SMVI has emerged as a particularly important factor to consider, correlating with disease recurrence and cancer-specific mortality. Additionally,
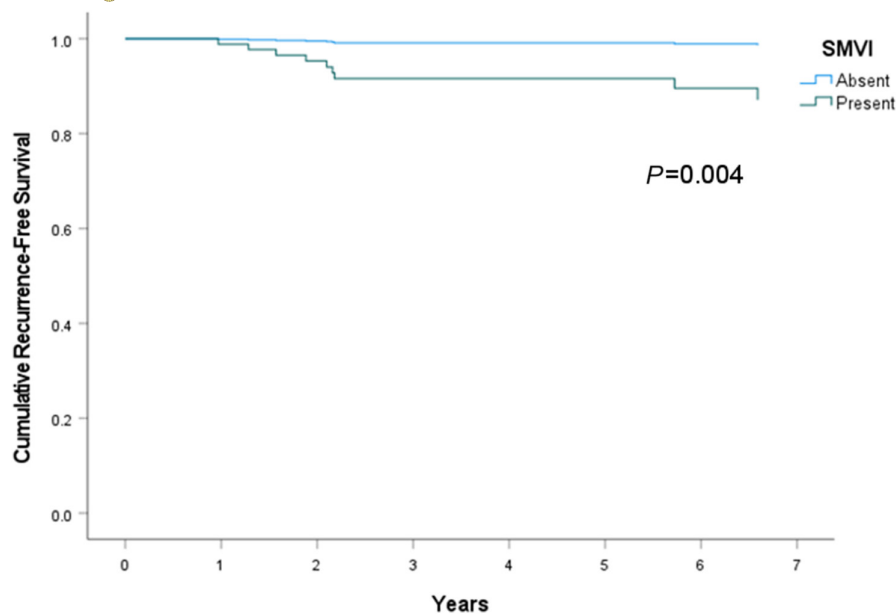
FIGURE 2 Relationship between SMVI and time to disease recurrence.
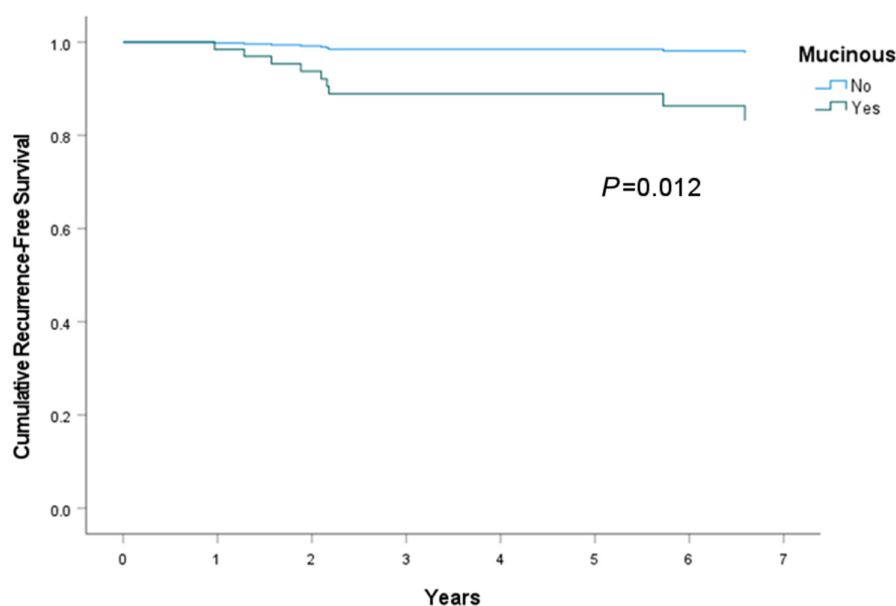
FIGURE 3 Relationship between mucinous subtype and time to disease recurrence.

mucinous subtype independently predicted recurrence, while poor differentiation independently predicted lymph node metastases. Conversely, the importance of polypectomy resection margin involvement has been brought into question. 94 of 153 (61.4%) patients initially managed with polypectomy had a positive margin. 38 belonged to group I (polypectomy only) with none developing recurrent disease, six belonged to group II (polypectomy followed by local excision of rectal scar) with no residual disease nor recurrence and 50 belonged to group III (polypectomy followed by surgical resection) with one found to have extramural venous invasion, one having residual malignant cells at the polypectomy site and three having involved lymph nodes. Thus only five of 94 (5.3%) with a positive polypectomy resection margin had evidence of locoregional residual tumour and only four of 94 (4.3%) developed long-term recurrence.

In recent history, the presence of high risk features prompted consideration for formal segmental resection using traditional surgical oncological principles including ensuring clear longitudinal and circumferential margins, with high vascular ties to include locoregional lymph nodes. However, recent paradigm shifts, particularly in the treatment of rectal cancer, are increasingly leading clinicians and patients toward the addition of systemic anticancer therapies, radiation or even moving to active surveillance strategies in place of radical resection in select cases [21]. The excellent long-term outcomes demonstrated in the current study among those undergoing local excision alone would appear to support conservative management strategies. As residual disease was rare in those with an apparently involved polypectomy resection margin, endoscopic surveillance and site check for early luminal recurrence seems a notably acceptable management option for such patients, in the absence of other

**TABLE 4** Cox regression analysis of factors associated with cancer-specific survival.

	CRC death		Univariate			Multivariate		
	No	Yes	HR	95% CI	P	HR	95% CI	P
Sex								
Male	130 (98%)	3 (2%)	1.0	0.307–6.201	0.675			
Female	99 (96%)	4 (4%)	1.380					
Age (years)								
Median (range)	68 (27–93)	65 (52–78)	0.993	0.921–1.071	0.857			
Location								
Colonic	158 (97%)	5 (3%)	1.0	0.174–4.623	0.896			
Rectal	71 (97%)	2 (3%)	0.897					
Morphology								
Pedunculated	68 (97%)	2 (3%)	1.0	0.216–5.784	0.895			
Sessile	161 (97%)	5 (3%)	1.117					
Polyp size								
<20 mm	113 (98%)	2 (2%)	1.0	0.500–13.362	0.257			
≥20 mm	116 (96%)	5 (4%)	2.586					
SMVI								
No	147 (99%)	2 (1%)	1.0	1.056–31.754	0.043			
Yes	53 (93%)	4 (7%)	5.792					
SMLI								
No	164 (97%)	5 (3%)	1.0	0.171–12.628	0.727			
Yes	22 (96%)	1 (4%)	1.468					
Poor differentiation								
No	199 (97%)	7 (3%)	1.0	–	0.690			
Yes	10 (100%)	0 (0%)	–					
Mucinous								
No	219 (97%)	6 (3%)	1.0	0.532–37.040	0.169			
Yes	10 (91%)	1 (9%)	4.438					
Margin ≤1 mm								
No	59 (100%)	0 (0%)	1.0	–	0.387			
Yes	90 (96%)	4 (4%)	–					
Excision								
Local	109 (99%)	1 (1%)	1.0	0.547–37.775	0.161			
Resection	120 (95%)	6 (5%)	4.547					

Abbreviations: CRC, colorectal cancer; HR, hazard ratio; SMLI, submucosal lymphatic invasion; SMVI, submucosal venous invasion.

risk factors. Furthermore, all six patients who proceeded from polypectomy to rectal scar excision had a positive polypectomy resection margin, but none was found to have evidence of local residual disease. MRI surveillance may be more difficult after such a rectal excision and perhaps this approach should be avoided, instead opting for surveillance or formal resection.

Given the low likelihood of locoregional disease, disease recurrence and CRC-related death in patients with T1 CRCs, overtreatment is a concern. Formal segmental resection carries the risk of perioperative morbidity, mortality or reduction in quality of life. In the large systematic review and meta-analysis by Yeh et al. [22] of 19 979 patients with T1 CRC, no significant difference was found between those undergoing endoscopic resection only and those proceeding directly to formal resection in recurrence-free survival (96.0% vs. 96.7%, HR 1.28, 95% CI 0.87–1.88), CSS (94.8% vs. 96.5%, HR 1.09, 95% CI 0.67–1.78) or overall survival (79.6% vs. 82.1%, HR 1.10, 95% CI 0.84–1.45). However, formal resection was associated with a significantly higher rate of procedure-related adverse events (10.9% vs. 2.3%; $P < 0.001$). Despite this, adopting an active surveillance strategy with frequent endoscopy and imaging over a number of years comes with its own concerns including patient acceptability, morbidity or psychological stress and the potential for under-staging in selected individuals with resultant local or distant recurrence. It is worth noting that four of 57 (7.0%) patients who proceeded from
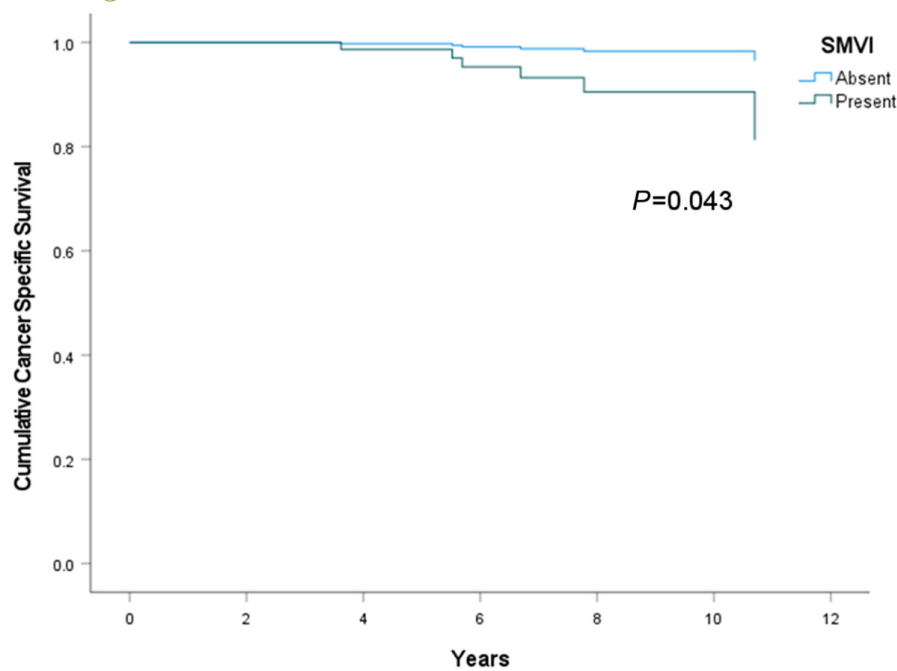
FIGURE 4 Relationship between SMVI and cancer-specific survival.

polypectomy to formal colorectal resection in this study developed disseminated malignancy while having no residual malignant cells found at the polypectomy site nor lymph node involvement. This highlights the unpredictable biology of a proportion of these early CRCs. The identification of novel factors which may enable risk stratification with greater accuracy would aid in the decision-making and, indeed, certain molecular signatures have been identified which correlate with risk of distant metastases [23].

Given the complexity of the decision-making it seems prudent that such cases are discussed at specialist CRC (MDT) meetings and, if possible, one focused on advanced polyps. Indeed, such an approach has been advocated by the Significant Polyp and Early Colorectal Cancer (SPECC) programme group [24]. The role of these MDTs should be to determine if endoscopic or local resection is technically possible and to estimate the associated risk of recurrence, with the ultimate management of that risk left to the patient in informed discussion with the surgeon. Such strategies may reduce the rate of segmental resection while ensuring no significant increase in local and distant disease recurrence or cancer-specific mortality. For patients who do not undergo bowel resection we would recommend the following surveillance protocol. For T1 rectal cancer which was macroscopically but not microscopically completely removed, we recommend a flexible sigmoidoscopy (to confirm absence of residual macroscopic tumour) and MRI scan (to look for mesorectal nodes) within 6 weeks and then 6 monthly for 2 years. If T1 rectal cancer is microscopically completely excised, 6 week flexible sigmoidoscopy is not necessary. If there are no risk factors for recurrence, follow-up MRI and flexible sigmoidoscopy are probably not necessary. For T1 colon cancer which was macroscopically completely removed but had a microscopically involved margin, we recommend a flexible sigmoidoscopy/colonoscopy (to confirm absence of residual macroscopic tumour) within 6 weeks. As recommended by the British

Society of Gastroenterology and Association of Coloproctology of Great Britain and Ireland post-polypectomy and post-colorectal cancer resection surveillance guidelines [5], all CRC patients should have colonoscopy at 1 and 3 years. All patients additionally should have surveillance for metastatic disease by CT chest, abdomen and pelvis at 1, 2 and 3 years and annual carcinoembryonic antigen check. If a patient is found to have luminal evidence of residual or recurrent disease, or if there is a suspicion of lymphadenopathy at MRI or CT surveillance, this prompts an immediate consideration for formal resection.

This study of patients undergoing treatment for T1 CRC is unique in its prospective nature with patients entered sequentially over 10 years and has a protracted follow-up. However, it must be noted that this is a purely observational study with no allocation of patients to a particular management pathway. Differences in characteristics and outcomes of the patients belonging to each management pathway have been reported, but the study did not seek to establish superiority of any pathway. There is inherent selection and reporting bias to a study of this type. Treatment decisions were made by a specialist colorectal oncology MDT, complemented by informed patient choice. As these decisions are complex, it is not possible to gauge what influence histological risk factors, patient age and comorbidity, potential for operative morbidity, tumour location and patient choice had on treatment allocation in each case. With a lack of standardized protocols or randomization of treatment there is likely to be allocation bias. However, the results represent heterogeneous real-world practice. Many of the key risk factors including SMVI, SMLI, submucosal depth and in particular Haggitt and Kikuchi levels were underreported. A key recommendation of this study is for universal reporting of these risk factors for T1 polyp CRCs. While the study size is large for a prospective cohort of this type, it is smaller than previously published retrospective studies. With a low number of events with regard to lymph node involvement, recurrence and cancer-specific

mortality, the study may be underpowered to detect significance in all risk factors assessed. However, our findings are largely concordant with larger retrospective studies, and we have filled an important gap in the literature in terms of prospective data with long follow-up. It is important that, as we adopt more conservative management approaches to the management of T1 CRC polyps, ongoing data collection and analysis is performed in a similar fashion to the current study to validate our findings and ensure no negative impact on outcomes.

CONCLUSIONS

Although 64.4% of those undergoing polypectomy alone had ≥1 recognized risk factor, there were no recurrences. Furthermore, only 5.3% of patients with a positive polypectomy margin had evidence of residual disease. Therefore, it seems feasible that those with a positive margin or single risk factor should be offered endoscopic surveillance. Further studies are required to confirm these findings. This study reinforces the importance of reporting SMVI, SMLI, submucosal depth, and Haggitt and Kikuchi levels for all T1 CRC polyps, and the findings highlight the need for discussion at sub-speciality MDTs to reduce unnecessary segmental resections and related morbidity, while ensuring effective surveillance and early salvage for those who recur. Patients should be offered a choice following an informed discussion.

AUTHOR CONTRIBUTIONS

Stephen McSorley: Methodology; supervision. **Andrew McMahon:** Conceptualization; methodology; supervision; investigation; data curation; project administration; formal analysis.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Caldicott Guardian approval was given by NHS GG&C to safeguard the record linkage with ethical approval waived for the purposes of service development.

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