The potential impact of local excision for T1 colonic cancer in elderly and comorbid populations: a decision analysis

Andrew C. Currie, MRCS,[1] Alan Askari, MRCS,[1] Christopher Rao, PhD, MRCS,[2] Brian P. Saunders, MD, FRCP,[3,4] Thanos Athanasiou, MD, PhD,[4] Omar D. Faiz, MS, FRCS,[1,4] Robin H. Kennedy, MS, FRCS[1,4]

Harrow, London, United Kingdom

Background: Population-based bowel cancer screening has resulted in increasing numbers of patients with T1 colonic cancer. The need for colectomy in this group is questioned due to the low risk of lymphatic spread and increased treatment morbidity, particularly for elderly, comorbid patients. This study examined the quality-of-life benefits and risks of endoscopic resection compared with results after colectomy, for low-risk and high-risk T1 colonic cancer.

Methods: Decision analysis using a Markov simulation model was performed; patients were managed with either endoscopic resection (advanced therapeutic endoscopy) or colectomy. Lesions were considered high risk according to accepted national guidelines. Probabilities and utilities (perception of quality of life) were derived from published data. Hypothetical cohorts of 65- and 80-year-old, fit and unfit patients with low-risk or high-risk T1 colonic cancer were studied. The primary outcome was quality-adjusted life expectancy (QALE) in life-years (QALYs).

Results: In low-risk T1 colonic neoplasia, endoscopic resection increases QALE by 0.09 QALYS for fit 65-year-olds and by 0.67 for unfit 80-year-olds. For high-risk T1 cancers, the QALE benefit for surgical resection is 0.24 QALYs for fit 65-year-olds and the endoscopic QALE benefit is 0.47 for unfit 80-year-olds. The model findings only favored surgery with high local recurrence rates and when quality of life under surveillance was perceived poorly.

Conclusions: Under broad assumptions, endoscopic resection is a reasonable treatment option for both low-risk and high-risk T1 colonic cancer, particularly in elderly, comorbid patients. Exploration of methods to facilitate endoscopic resection of T1 colonic neoplasia appears warranted. (Gastrointest Endosc 2016;84:986-94.)

INTRODUCTION

Colectomy provides the opportunity for complete resection and accurate staging of disease and is the current standard of care in early colonic cancer. However, risks of morbidity and mortality remain significant even within enhanced recovery and laparoscopic practice,[1] with greater risk for elderly, comorbid patients.[2] In recent years, local excision techniques, such as advanced endoscopic resection, have evolved to treat complex colonic polyps and early carcinoma. These endoscopic therapies include EMR and endoscopic submucosal dissection (ESD),[3] which are much less invasive procedures than colectomy. Recent evidence demonstrates that polyp surface pattern assessment[4] and colonoscopic miniprobe US[5] can accurately identify T1 colonic malignancy. Although endoscopic therapy cannot resolve the problem of lymph node metastases, data from Japan indicate T1 cancers with submucosal invasion <1000 μm and >1000 μm have lymph node

Abbreviations: ESD, endoscopic submucosal dissection; HES, Hospital Episode Statistics dataset; JSCCR, Japanese Society for Cancer of the Colon and Rectum; NHS, National Health Service; QALE, quality-adjusted life expectancy; QALY, quality-adjusted life year; SD, standard deviation; SEER, Surveillance, Epidemiology, and End Results Program.

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Current affiliations: Department of Surgery, St Mark's Hospital and Academic Institute, Harrow, Middlesex (1), Department of Surgery, Queen Elizabeth Hospital, Woolwich, London (2), Wolfson Department of Endoscopy, St Mark's Hospital and Academic Institute, Harrow, Middlesex (3), Department of Surgery and Cancer, Imperial College London, London, UK (4).

Reprint requests: Andrew Currie, MRCS, St. Mark's Hospital, Watford Road, Harrow, Middlesex HA1 3UJ, UK.

metastases in 0% and 12.9%, respectively.[6] This suggests that endoscopic resectional techniques for T1 colonic cancer may be curative for many patients. Many surgeons still prefer colectomy to endoscopic resection because they are concerned that recurrent disease is more likely and may affect long-term survival. Therefore, in a patient with early colonic adenocarcinoma, the benefits of a relatively noninvasive advanced endoscopic or other local excision procedure have to be weighed against the associated risk of missing the opportunity for cure. Patient comorbidity increases the risk of post-operative adverse events, making the decision particularly complex. The ability to combine the inherent risks associated with elderly age and comorbidity with the potential outcomes of 2 competing techniques is a particular strength of decision modeling.[7]

Aims

The aim of the present study was to evaluate the best treatment strategy for patients with early colonic cancer. Using a decision analysis, we have compared the effectiveness of endoscopic resection and surgical resection in T1 colonic malignancy.

METHODS

Model structure

A Markov model is a recursive decision analysis that guides a hypothetical cohort between mutually exclusive health states depending on transition probabilities defined from published literature. Decision analytical modeling using Markov simulation was used to investigate the health benefits (quality-adjusted life expectancy [QALE]) accruing to patients with T1 colonic cancer treated either with endoscopic resection, using advanced endoscopic resection, or colectomy. The model structure is based on a previous study comparing the watch-and-wait approach with radical surgery in rectal cancer after complete clinical response from pre-operative radiotherapy.[7] In the model, simulated patients undergo endoscopic resection or colectomy as a primary approach (Fig. 1). Our model comprised 4 different hypothetical patient groups: a 65-year-old male cohort with no or minimal comorbidity (Charlson Score <3) (fit65), an 80-year-old male cohort with no or minimal comorbidity (fit80), a 65-year-old male cohort with significant comorbidities (Charlson Score ≥3) (com65), and an 80-year-old male cohort with significant comorbidities (com80). These scenarios were chosen because existing studies suggest morbidity and mortality associated with colorectal resection is significantly increased after the age of 70 years.[8] The Charlson Comorbidity Index is an established tool to predict mortality for patients with comorbid conditions.[9]

For simulation purposes, the diagnosis of T1 colonic cancer, either low-risk or high-risk, was based on prior endoscopic findings, including narrow-band imaging, chromoendoscopy, and miniprobe US and was assumed to be accurate. Distant metastatic disease has been excluded with a CT scan. According to the Japanese Society of Colorectal Cancer (JSCCR) guidelines, patients were considered to have high-risk T1 lesions if they had histologic features of poor differentiation, submucosal invasion (>1000 μm), lymphovascular invasion, a positive resection margin, or grade 2 or 3 tumor budding. We developed the decision analysis model using TreeAge Pro 2015 software (TreeAge Software, Inc, Williamstown, Mass).

Model inputs/data sources

A comprehensive literature search was performed to identify the probability of clinical events. Six studies including 1259 patients were identified that categorized T1 colorectal cancers according to the JSCCR guidelines (or used similar criteria) as either low-risk or high-risk lesions.[10-15] These studies all reported on patients who had advanced therapeutic endoscopic resection only, or had a subsequent or primary colectomy. All base case values and probability distributions used in the model and data sources are shown in Table 1. For the purposes of the model, it was assumed that the oncologic outcomes for T1 colonic neoplasia were equivalent to the T1 colorectal data from these studies.

Mortality in the immediate 90 days and first year after resection for each demographic cohort was obtained from the Hospital Episode Statistics (HES) database, a routinely collected administrative dataset, which captures clinical activity for all patients treated in English National Health Service (NHS) hospitals.[16] HES data are widely used for NHS quality assurance by government agencies and in the academic literature.[17] Baseline mortality outcome was derived from the UK Office of National Statistics Life Tables.[18] Adjustments for comorbidity levels were applied according to the formulas of Mariotto et al.[19] Cancer survival was taken from the Surveillance, Epidemiology, and End Results Program (SEER) database.[20]

Treatment approaches

For the endoscopic resection arm of the model, data for patients undergoing primary advanced endoscopic resection of a T1 colorectal cancer were used; colonic lesions were assumed to carry similar technical and oncological risks as colorectal lesions. A primary endoscopic resection approach will have to be converted to colectomy in 10% to 15% of patients because of technical challenges or a procedural verse event.[3,21] We included those patients who were converted immediately to colectomy in the endoscopic treatment arm in an intention-to-treat analysis. Surveillance after both endoscopic resection and surgery was assumed to be intensive in order to identify treatable recurrent disease.

Recurrence

Survival and quality of life after local recurrence was assumed to be equivalent to Union International for

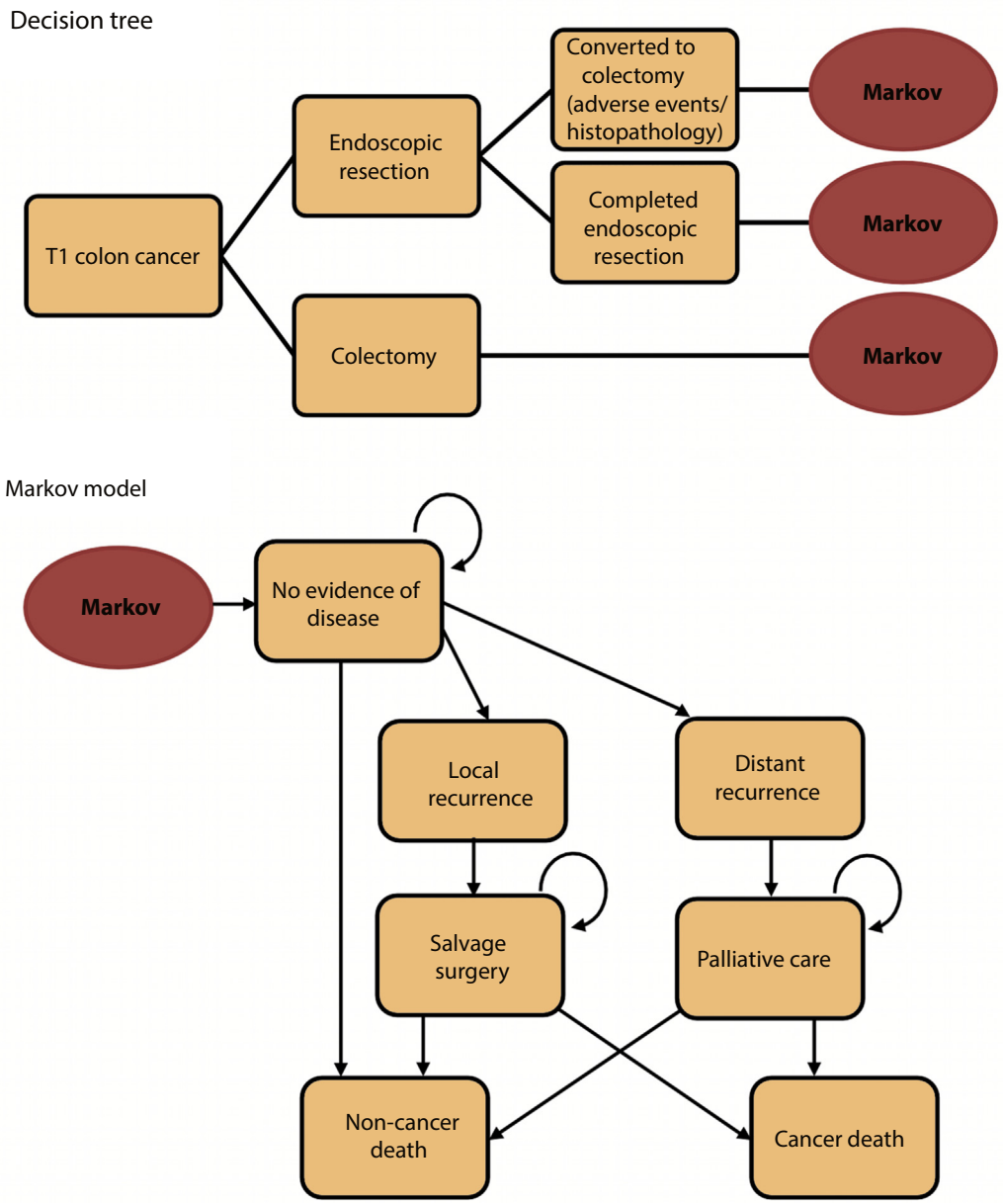

Figure 1. Model structure.

Cancer Control (UICC) stage III cancer at diagnosis. The model assumed that should local recurrence occur, all patients would undergo salvage surgery. If distant recurrence occurred, it was assumed that survival and quality of life were equivalent to UICC stage IV cancer at presentation, and palliative management was instituted. For both colectomy and endoscopic resection, recurrence was assumed to occur within 5 years after the initial intervention.

Utilities

A utility is a weight assigned to an individual's preference for a particular health state, with a range between 0 (death) and 1 (perfect health). Quality-adjusted life-years (QALYs) are generated when this weight is applied to a year of life in the health state described; ie, a higher QALY reflects a year of life in a preferred health state. For the post-surgical and recurrence states, utilities were elicited from patients with proven colorectal adenomas using the time–trade-off method, in which individuals are asked to define the amount of time they would be willing to sacrifice to be in a better health state versus a poorer health state.[22] For the post-endoscopic resection utility, the study modeled a minimal reduction in quality of life.[23] The utility during follow-up was assumed to be the same for post-colectomy and post-endoscopic resection patients from 1 year onward, and the quality of life

TABLE 1. Model probabilities and utilities

Model parameter	Mean (SD)*	Distribution for PSA	Sources
90-day post-operative mortality after colectomy†			HES
Fit 65-year-old	0.013 (0.001)	Beta (α, 77; β, 5765)	
Fit 80-year-old	0.060 (0.025)	Beta (α, 172; β, 2686)	
Comorbid 65-year-old	0.034 (0.026)	Beta (α, 57; β, 1630)	
Comorbid 80-year-old	0.097 (0.044)	Beta (α, 80; β, 746)	
90-day post-procedural mortality after local excision†			HES
Fit 65-year-old	0.003 (0.001)	Beta (α, 27; β, 8945)	
Fit 80-year-old	0.015 (0.019)	Beta (α, 36; β, 2432)	
Comorbid 65-year-old	0.010 (0.037)	Beta (α, 3; β, 301)	
Comorbid 80-year-old	0.039 (0.063)	Beta (α, 7; β, 172)	
Chance of failure of primary local excision	0.15 (0-0.4)‡	Triangular	2,19
Recurrence after primary local excision (5-year) for low-risk T1	0.009 (0-0.040)‡	Triangular	10-15
Recurrence after primary colectomy (5-year) for low-risk T1	0 (0-0.200)‡	Triangular	10-15
Recurrence after primary local excision (5-year) for high-risk T1	0.097 (0-0.1800)‡	Triangular	10-15
Recurrence after primary colectomy (5-year) for high-risk T1	0.021 (0-0.050)‡	Triangular	10-15
% of recurrences that are local if primary local excision	0.85 (0.75-1)‡	Triangular	10-15,25
% of recurrences that are local if primary colectomy	0.2 (0-0.75)‡	Triangular	10-15,5
Surgical mortality after salvage surgery for local recurrence (1 year)†			HES
Fit 65-year-old	0.035 (0.002)	Beta (α, 207; β, 5635)	
Fit 80-year-old	0.120 (0.029)	Beta (α, 344; β, 2514)	
Comorbid 65-year-old	0.135 (0.036)	Beta (α, 228; β, 1459)	
Comorbid 80-year-old	0.270 (0.054)	Beta (α, 223; β, 603)	
Annual relative survival after local recurrence with surgical salvage	0.0699 (0.0088)	Beta	SEER[18]
Annual relative survival with distant metastatic disease	0.3467 (0.0434)	Beta	SEER[18]
Utility of local excision (up to 1 year post-procedure)	0.99 (0.01)	Beta	21
Utility of colectomy (up to 1 year post-operative)	0.74 (0.20)	Beta	20
Utility for local recurrence with associated morbidity	0.67 (0.23)	Beta	20
Utility for distant recurrence with associated morbidity	0.25 (0.25)	Beta	20

SD, Standard deviation; *PSA*, probabilistic sensitivity analysis; *HES*, Hospital Episode Statistics dataset; *SEER*, Surveillance, Epidemiology, and End Results Program.
*Unless otherwise stated.
†Because mortality rates were described by beta distributions, means and SD are presented for representative purposes only: mean $= \alpha/\alpha + \beta$; SD $= \sqrt{(\alpha\beta/[\alpha + \beta]^2[\alpha + \beta + 1])}$.
‡Mode (minimum-maximum).

reduction was assumed to be negligible.[24,25] In the model, patients maintain post-treatment utilities until death, unless they develop cancer recurrence. QALYs were calculated with a lifetime horizon. An annual discount rate of 3.5% was applied to all pay-offs in the QALY model.

Sensitivity, threshold, and probabilistic sensitivity analyses

We conducted 1-way sensitivity analyses to define thresholds around key variables. Threshold analyses were performed to identify probability and utility values at which the optimal strategy (defined by the highest QALE) changed.

We also performed a probabilistic sensitivity analysis using a Monte Carlo simulation,[26] in which the uncertainties of all transition probabilities were considered simultaneously from 10,000 iterations. Uncertainty around event probabilities and utilities was represented using β distributions (Table 1) except for uncertainty around the probabilities of failure of primary endoscopic resection and developing recurrence after either treatment, which were estimated using triangular distributions.

RESULTS

Quality-adjusted life expectancy

In low-risk T1 colonic neoplasia, the endoscopic resection approach derives a QALE of 20.22, 11.80, 12.40, and 5.58 years for the fit65, fit80, com65, and com80 cohorts, with an increase in QALE of 0.09 (0.4%), 0.38 (3.2%),

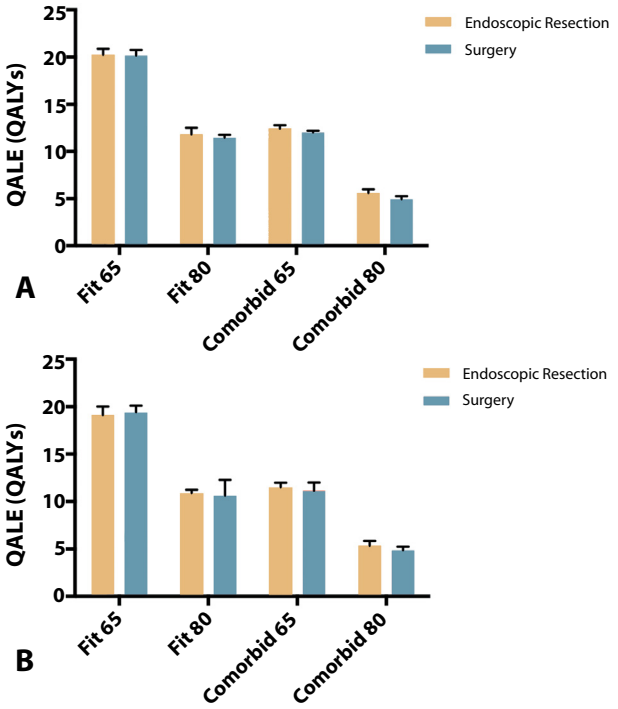

Figure 2. Comparative life quality-adjusted life expectancy (QALE) for patients with (**A**) low-risk and (**B**) high-risk T1 colon cancer managed by endoscopic resection or colectomy. Median and 95% credible interval data shown. *QALY*, quality-adjusted life-year.

0.42 (3.4%), and 0.67 (12.0%) years, respectively (Fig. 2). For high-risk T1 cancers, the QALE produced by the endoscopic approach was 19.12 years (fit65), 10.85 years (fit80), 11.45 years (com65), and 5.32 years (com80), with a QALE improvement from the endoscopic approach of 0.28 (2.6%), 0.32 (2.8%), and 0.47 (8.8%) QALYs for the fit80, com65, and com80 populations, respectively. For the fit65 cohort with high-risk cancer, the surgical approach (19.36 years) offered a QALE advantage of 0.24 (1.2%) QALYs. For all populations, QALE was greater for low-risk T1 lesions because of the lower QALYs associated with recurrence. There was a reduction in QALE projection with increasing age and comorbidity for both T1 lesion types, consistent with general reductions in overall life expectancy. The probabilistic sensitivity analysis revealed that the endoscopic resection approach was favored in the majority of simulations across both T1 risk levels and in all populations. For the low-risk T1 group, the endoscopic resection approach was favored in 65%, 73%, 74%, and 78% of simulations in the fit65, fit80, com65, and com80 cohorts. For the patients with high-risk T1 lesions, the endoscopic resection approach was preferred in 45%, 67%, 68%, and 71% of the fit65, fit80, com65, and com80 cohorts.

Overall survival

The projected overall survival is shown in Table 2. As patients aged and became more comorbid, overall survival reduced in both the low-risk and high-risk cancer cohorts. For low-risk cancers, the local excision approach offered a predicted survival benefit at all time points and in all cohorts. For high-risk lesions, predicted overall survival was slightly better with a local excision approach for the fit80, com65, and com80 cohorts, whereas surgery offered a small improvement in predicted overall survival for the fit65 cohort.

Disease-free survival

The projected disease-free survival is shown in Table 2. There was a reduction in disease-free survival with increasing age and morbidity for both low-risk and high-risk T1 cancer populations. For the low-risk cancer group simulations, local excision offered improved disease-free survival for all populations for up to 5 years. For the fit65, fit80, and com65 high-risk cancer populations, surgery had a better disease-free survival from the 3-year time point. For the com80 group, local excision had better disease-free survival up to 5 years.

Sensitivity analysis

The findings of the QALE analysis were sensitive to variations in the following parameters within their plausible range: probability of recurrence after endoscopic resection, 90-day mortality after endoscopic resection and colectomy, and utility of living in the post-endoscopic resection and post-colectomy states (Table 3). The thresholds of probability of recurrence after endoscopic resection identified for preferring primary surgery are significantly higher than the observed weighted mean average recurrence rates in the comparative studies. The mortality rates after endoscopy and colectomy required to favor surgical resection were at the extremes of the plausible ranges used in the sensitivity analysis.

DISCUSSION

Endoscopic resection appears to potentially increase QALE in patients with low-risk or high-risk T1 colonic cancer, particularly for the elderly and those with comorbidity. This analysis further demonstrates that when a broad spectrum of possible disease and quality of life–related outcomes are measured, then an endoscopic resection remains a reasonable potential approach in patients with either low-risk or high-risk T1 colonic neoplasia. The 5-year overall survival data (approximately 95% for the fit population) are in agreement with the outcomes from the 6 studies used to populate the model[10-15] as well as international cohorts,[27] indicating the validity of this decision model.

Few studies have reported on comparative outcomes between radical surgery and an endoscopic resectional approach for T1 colonic cancer. In a retrospective study of around 600 T1 cancers, Kiriyama et al[28] found that

TABLE 2. Predicted disease-free and overall survival for local excision and colectomy for T1 colonic cancer

Cohort (cancer type/ comorbidity/age)	Treatment	Disease-free survival			Overall survival		
		1 year	3 years	5 years	1 year	3 years	5 years
Low-risk							
Fit65	Endo	0.98 (0.97-0.99)	0.96 (0.94-0.97)	0.93 (0.91-0.95)	0.99 (0.98-0.99)	0.97 (0.95-0.98)	0.92 (0.90-0.94)
	Surg	0.98 (0.96-0.99)	0.96 (0.94-0.97)	0.93 (0.91-0.95)	0.98 (0.97-0.99)	0.96 (0.95-0.97)	0.93 (0.92-0.94)
Fit80	Endo	0.94 (0.92-0.96)	0.87 (0.84-0.89)	0.78 (0.75-0.81)	0.94 (0.93-0.95)	0.87 (0.86-0.88)	0.79 (0.78-0.80)
	Surg	0.91 (0.89-0.93)	0.84 (0.81-0.86)	0.76 (0.73-0.78)	0.91 (0.90-0.92)	0.84 (0.83-0.85)	0.76 (0.75-0.77)
Com65	Endo	0.94 (0.92-0.96)	0.86 (0.83-0.88)	0.78 (0.74-0.81)	0.93 (0.94-0.95)	0.86 (0.85-0.87)	0.78 (0.77-0.79)
	Surg	0.92 (0.91-0.94)	0.85 (0.82-0.87)	0.77 (0.74-0.79)	0.92 (0.91-0.94)	0.85 (0.84-0.86)	0.77 (0.76-0.78)
Com80	Endo	0.85 (0.82-0.88)	0.66 (0.62-0.69)	0.47 (0.43-0.51)	0.85 (0.83-0.87)	0.66 (0.64-0.68)	0.48 (0.46-0.49)
	Surg	0.81 (0.78-0.84)	0.63 (0.59-0.66)	0.45 (0.42-0.48)	0.81 (0.79-0.83)	0.63 (0.61-0.65)	0.46 (0.44-0.47)
High-risk							
Fit65	Endo	0.97 (0.95-0.98)	0.92 (0.88-0.96)	0.87 (0.81-0.93)	0.99 (0.98-0.99)	0.96 (0.94-0.97)	0.92 (0.90-0.94)
	Surg	0.97 (0.96-0.98)	0.95 (0.93-0.96)	0.92 (0.98-0.94)	0.98 (0.97-0.98)	0.96 (0.95-0.97)	0.93 (0.92-0.94)
Fit80	Endo	0.93 (0.90-0.95)	0.83 (0.79-0.87)	0.73 (0.67-0.78)	0.94 (0.93-0.95)	0.86 (0.85-0.87)	0.77 (0.75-0.79)
	Surg	0.90 (0.88-0.92)	0.83 (0.80-0.85)	0.74 (0.71-0.78)	0.91 (0.90-0.92)	0.84 (0.83-0.85)	0.76 (0.74-0.77)
Com65	Endo	0.93 (0.90-0.95)	0.82 (0.78-0.86)	0.72 (0.67-0.78)	0.94 (0.92-0.96)	0.86 (0.85-0.87)	0.76 (0.74-0.78)
	Surg	0.92 (0.90-0.94)	0.84 (0.81-0.86)	0.75 (0.72-0.78)	0.92 (0.91-0.94)	0.85 (0.83-0.86)	0.76 (0.75-0.78)
Com80	Endo	0.84 (0.80-0.87)	0.63 (0.58-0.67)	0.44 (0.39-0.49)	0.85 (0.83-0.87)	0.65 (0.64-0.67)	0.46 (0.44-0.48)
	Surg	0.81 (0.78-0.84)	0.62 (0.59-0.66)	0.44 (0.41-0.48)	0.81 (0.79-0.83)	0.63 (0.61-0.65)	0.45 (0.44-0.47)

Data quoted as median (95% credible intervals).
Endo, Endoscopic (local excision); *Surg*, surgical (colectomy).

patients treated with ESD had 3-year survival rates comparable with those undergoing laparoscopic colorectal resection (99.2% and 99.5%, respectively). However, the laparoscopically resected group had a much higher proportion of advanced T1 cancers (sm2 or deeper) (70% vs 15% for the endoscopic resection group) indicating possible selection bias. An analysis of the SEER database demonstrated that T1 colon cancers have comparable overall and disease-free survival regardless of local or radical resection.[27] However, neither study addressed patient comorbidity assessment and quality-of-life factors, which are known to be vital for patient decision making in this area.[29] The lack of randomized evidence and the considerable uncertainty in this area of surgical practice means clinicians are heavily guided by clinical practice guidelines for the management of early colorectal cancer. Although the JSCCR guidelines state that an endoscopic or local resection approach is sufficient for low-risk T1 colon cancer, it proposes a more radical approach to high-risk lesions. This study demonstrates that even for high-risk lesions, quality of life and competing surgical mortality hazards can make endoscopic resection approaches appropriate.

The challenge of conducting randomized trials in early colorectal cancer has led to the development of other recent decision analytic models comparing local treatments with radical resection. Johnston et al[30] compared QALE between transanal local excision and abdominoperineal excision for low rectal T1 cancers and found that a local excision approach would result in around 1 QALY benefit for their base case 65-year-old patient. Smith et al,[7] using a model structure similar to this study, evaluated the impact of a watch-and-wait approach in rectal cancer after complete clinical response from pre-operative radiotherapy. They found significant increases in early overall survival for observation over radical rectal resection in the elderly, comorbid population. These models and the current study indicate that the morbidity and mortality from radical resection govern treatment selection and that local excisional approaches should also be considered in T1 colonic malignancy.

There are limitations to any model-based study, because it is dependent on the inputted parameters. The main limitation of the recurrence data used for this study is that much of it is derived from only a small number of studies pertaining to a highly selected group of patients. ESD is predominantly performed in Japan and other Eastern centers. Although a few selected European centers are undertaking ESD, a considerable amount of work is required for even those centers to surmount the learning curve. To allow for this complexity, our sensitivity analysis varied failure of endoscopic resection in up to 40% of cases (well in excess of rates reported in the literature) and still found that endoscopic resection was preferred. However, because there are few studies of endoscopic resection of T1 colonic malignancy, this failure rate has been estimated

TABLE 3. One-way sensitivity analysis for quality-adjusted life expectancy comparing local excision and colectomy for T1 colon cancer

Variable	Cancer type	Population	Base case value (%)	Range tested in sensitivity analysis (%)	Threshold to favor surgery (%)
90-day post-colectomy mortality	Low-risk	Fit65	1.3	0.0-25.0	No threshold
		Fit80	6.0	0.0-25.0	No threshold
		Com65	3.5	0.0-25.0	No threshold
		Com80	9.7	0.0-25.0	No threshold
	High-risk	Fit65	1.3	0.0-25.0	<1.0
		Fit80	6.0	0.0-25.0	<2.2
		Com65	3.5	0.0-25.0	<2.4
		Com80	9.7	0.0-25.0	No threshold
90-day post-endoscopy mortality	Low-risk	Fit65	0.3	0.0-25.0	≥1.8
		Fit80	1.5	0.0-25.0	≥4.8
		Com65	1.0	0.0-25.0	≥4.5
		Com80	3.9	0.0-25.0	≥13.0
	High risk	Fit65	0.3	0.0-25.0	≥13.8
		Fit80	1.5	0.0-25.0	≥23.5
		Com65	1.0	0.0-25.0	≥22.1
		Com80	3.9	0.0-25.0	≥30.5
5-year recurrence risk after endoscopic resection	Low-risk	Fit65	0.9	0.0-25.0	≥5.2
		Fit80	0.9	0.0-25.0	≥7.1
		Com65	0.9	0.0-25.0	≥6.7
		Com80	0.9	0.0-25.0	≥22.0
	High-risk	Fit65	9.7	0.0-50.0	≥15.3
		Fit80	9.7	0.0-50.0	≥28.9
		Com65	9.7	0.0-50.0	≥26.8
		Com80	9.7	0.0-50.0	≥46.8
Post-colectomy utility	Low-risk	Fit65	0.74	0.50-1.00	No threshold
		Fit80	0.74	0.50-1.00	No threshold
		Com65	0.74	0.50-1.00	No threshold
		Com80	0.74	0.50-1.00	No threshold
	High-risk	Fit65	0.74	0.50-1.00	>0.95
		Fit80	0.74	0.50-1.00	No threshold
		Com65	0.74	0.50-1.00	No threshold
		Com80	0.74	0.50-1.00	No threshold
Post-endoscopic resection utility	Low-risk	Fit65	0.99	0.00-1.00	<0.67
		Fit80	0.99	0.00-1.00	<0.53
		Com65	0.99	0.00-1.00	<0.58
		Com80	0.99	0.00-1.00	<0.40
	High-risk	Fit65	0.99	0.00-1.00	<0.76
		Fit80	0.99	0.00-1.00	<0.66
		Com65	0.99	0.00-1.00	<0.68
		Com80	0.99	0.00-1.00	<0.49

Only the factors that demonstrated a threshold are shown in the table. All other variables examined did not influence the treatment decision.

from the need for salvage colectomy in studies of polyp resection for the current model, and further experience may alter the probabilities of failure. In addition, the complexity of the approach indicates that any proposal to expand endoscopic resection of T1 colonic cancer will likely require centralization of practice in a few selected centers for quality and training purposes. We have further hypothetically assumed the ability to accurately define

T1 high-risk and low-risk lesions before resection. We have not modeled the risk of including T2 or more advanced cancers in either treatment arm because no data were available on T2 cancer outcomes after endoscopic resection. Although current staging practices in general hospitals are not sufficiently accurate, work on colonoscopic EUS indicates selected specialist centers could facilitate accurate local T1 colon cancer staging.[5] Some data from small series indicate that colonoscopic EUS can differentiate between T1sm3 and T2 lesions,[31,32] but this requires verification in larger, multicenter cohorts. Furthermore, we included data only from studies where primary endoscopic resection had been undertaken and the data on surgical patients were taken from patients having colorectal resection after advanced endoscopic resection of a T1 cancer. However, our use of cohort studies using JSCCR guidelines to attribute oncologic risk has reduced the heterogeneity in cancer outcomes seen within the T1 colon cancer population. The assumption has been made in this study that procedural endoscopic capability and risk as well as oncologic outcome are comparable between rectal and colonic lesions because there is currently limited evidence to suggest any disparity.[3,33] Although this assumption may be disputed, the evidence surrounding the differences is limited, and practice in both colon and rectal lesions is influenced by similar data. Despite these limitations, this decision analysis assimilates the best available data on the important factors governing decision making in T1 colon cancer, and our thorough sensitivity analyses addresses the considerable uncertainty in the field. Finally, the relevance of comparing UK administrative data with other health care systems may be questioned,[34] but the sensitivity analysis reducing post-operative mortality rates to artificially low levels, our use of 90-day mortality to accurately assess the impact of post-procedural intermediate mortality,[35-37] and the considerable international evidence indicating mortality rates after colorectal surgery are under-recognized, particularly in the elderly,[38] suggest that this approach is appropriate.

Significant changes in clinical practice will be required to implement the findings of this decision model. Data from regional practice in northern England have shown that biopsies were performed for about 50% of T1 colorectal cancers and discussed in a multidisciplinary meeting (tumor board), with the remainder proceeding directly to endoscopic resection, indicating in most cases that these were presumed benign.[39] To enable all patients to have the opportunity to have an informed consultation regarding the benefits and risks of endoscopic resection versus colectomy will require improved pre-operative recognition and local staging of early colon cancer. Improved education will be necessary on local endoscopic staging practices, such as pit pattern recognition, which have been shown to be within the remit of non-specialist endoscopists.[4] Further it will require the formation of clinical practice networks where patients with complex or presumed malignant polyps can be referred to specialist centers for enhanced assessment and management. These networks are already advocated for complex, benign colonic lesions, and they have been shown to reduce the need for colectomy.[40-42] In addition, centralization would be required so that ESD or other local colonic excision could be offered to all patients. ESD has been predominantly developed in Japan, with few European centers reporting experience.[43] For quality and training purposes, ESD should continue to be offered only in selected centers with appropriate experience and audited outcomes. Alternatively, new techniques, such as full-thickness endoscopic[44] or laparoendoscopic[45] excision, in the colon may become available in widespread clinical practice. Despite these practice barriers, this decision model indicates that considerable patient benefits could be derived from an endoscopic resection approach to T1 colon cancer.

The results of this study demonstrate that endoscopic resection for patients with a T1 colonic cancer may result in improved quality of life outcome when compared with radical surgery, especially in elderly, comorbid patients. These results are mediated through the avoidance of surgical risk, and persist for patients with low-risk and high-risk lesions defined by the Japanese criteria. This study supports increasing focus on the role of local excision in T1 colonic cancer, particularly in elderly, comorbid patients, and paves the way for future clinical trials.

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