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The Malignant Polyp: Polypectomy or Surgical Resection?

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1. Introduction

Endoscopic resection of colorectal polyps is a well-recognised therapy for the prevention of colorectal carcinoma. Roughly 10% of resected polyps contain foci of carcinoma and are often termed malignant polyps or polyp cancers. Their incidence is increasing in line with the increasing use of colonoscopy.[1] A proportion of these will have progressed to nodal disease before presentation and a further oncological resection should be considered for high risk patients.[2]

The risk of nodal disease at presentation can be stratified by histology but definitive staging information can currently only be obtained by oncological resection, a procedure which can cause significant morbidity and mortality, especially in the elderly. This is of particular relevance as the majority of patients do not have nodal disease, even for the most dangerous categories of polyp.[3] There is a real risk of causing excess morbidity by over treating the majority in order to adequately treat the minority.

2. Malignant polyps

Not all polyps are created equal. The adenoma carcinoma sequence has long been recognised as the natural history of colorectal carcinoma and it is therefore logical that some adenomas will be discovered with foci of malignancy within them.

For those confined to the mucosa, polyps showing foci of potentially malignant cells are often termed *carcinoma in situ*. The lack of lymphatics in the mucosa prevents distant spread and, as these lesions are neither regarded as malignant or treated as malignancies, the term high grade mucosal neoplasm is now preferred. [4]

The definition of colorectal carcinoma is dysplasia crossing the *muscularis mucosa*, so when high grade dysplasia in these polyps crosses this barrier the lesion is termed a malignant polyp. A malignant polyp is essentially a macroscopically benign lesion that contains malignant foci on further examination. When the totality of the polyp is comprised of malignancy the term polypoid carcinoma is often used.

T1 lesions are therapeutically significant as they are the first lesions where nodal and distant metastases must be considered. The management of these polyps is based on the belief that the risk of spread can be stratified according to the histology of the resected polyp.[5] In the past authors used various criteria to define favourable or unfavourable histology and guide management.[1,2,6,7] For a large part, this has involved dividing patients into two groups. A “low risk” group, who are safe without further treatment and a “high risk group”, for whom surgery should be considered.[8,9] Unfortunately published studies disagree about the factors that are most significant.[3,10-12]

3. Factors affecting risk of nodal disease

3.1. Morphology

The Paris classification[13] of gastro-intestinal tumours recognises that adenomas may be polypoid or non polypoid. Non polypoid (0-II, 0-III) lesions are not usually removed endoscopically as they are more challenging to remove and are recognised to have high malignant potential.

0-I: Polypoid	0-Ip: Pedunculated
	0-Is: Sessile
0-II : Non-Polypoid, Non Ulcerated	0-IIa: Slightly elevated
	0-IIb: Flat
	0-IIc: Slightly depressed
0-III: Ulcerated	

Table 1. Paris Classification of Superficial Tumours of the Colon and Rectum.[13]

Polypoid lesions can be pedunculated (Type 0-1p) or sessile (Type 0-1s). Due to their shape malignant sessile polyps are harder to remove with clear margins and have more ready access to the deeper portions of the submucosa. They are therefore more likely to be classified as high risk. Seitz et al[9] presented a series of 114 endoscopically removed malignant polyps. Overall 46% of these polyps were sessile, but 65% of “high risk” (ie. requiring surgical removal) polyps were sessile. Conversely only 23% of “low risk” polyps were sessile.

An earlier literature series of 741 malignant polyps reported that 58.3% of sessile polyps had “high risk features” (Grade 3-4, vascular or lymphatic invasion, positive resection margin)

whereas only 10% of pedunculated polyps were similarly classified.[11] One meta-analysis reported positive resection margins in 56.8% of sessile lesions versus 18.7% in polypoid lesions ($P < 0.0001$).

Size and tubular or villous architecture are also well known to affect the malignant potential of polyps. However, in a similar fashion to flat or depressed areas of dysplasia, very large polyps are seldom excised endoscopically and are not relevant to the current topic.

3.2. Grading

Polyps are defined by dysplasia and the varying degree displayed by different polyps is thought to explain a large degree of their different metastatic potential.[14]

Negative for Intraepithelial neoplasia.	
Indefinite for Intraepithelial neoplasia.	
Low-grade Intraepithelial neoplasia.	Adenoma/dysplasia
High-grade neoplasia (intraepithelial or intramucosal)	Adenoma/dysplasia (4-1)
	Noninvasive carcinoma (4-2)
	Suspicious for invasive carcinoma (4-3)
	Intramucosal carcinoma (lamina propria invasion) (4-4)
Submucosal carcinoma	

Table 2. Revised Vienna classification of epithelial neoplasia for esophagus, stomach, and colon. [13]

The revised Vienna classification is widely used to define the degree of dysplasia colorectal polyp. By definition malignant polyps are 4-4. For colorectal carcinomas the WHO classification recognises 4 grades of differentiation, with G1 representing well differentiated, through moderate (G2) and poorly differentiated (G3) to undifferentiated (G4). G1-2 are conventionally regarded as low grade and G3-4 as high grade.

In a meta-analysis of published series, Hassan *et al.*[1] reported a 3.9 (1.9-8.4) odds ratio for nodal metastasis with regard to high vs low grade malignant polyps. The odds ratio for mortality was reported as 9.2 (4.7-18.2). Determining the exact risk from high grade dysplasia is complicated by their relative rarity. One study of 80 malignant polyps found only 2 poorly differentiated polyps.[12] In a meta-analysis 7.2% of 1612 malignant polyps were high grade.[1]

It is interesting to note that despite poor differentiation being recognised as an important determinant of nodal disease, no universally accepted definition exists. Indeed in studies where the prevalence of highly dysplastic lesions was lower, the risk of nodal disease in these polyps was increased. (See Table 3). This suggests that poor differentiation, when a rigorous definition is used is an extremely important predictor of nodal disease. Those studies that did not find the degree of dysplasia to be significant are hampered by the very small number of highly dysplastic lesions in their sample.

Study	Number Of T1 Tumours	Incidence of G3 Poorly Differentiated/% (No. of Cases)	Incidence of Nodal Involvement / % (No. of Cases)
Yamamoto et al 2004	301	0.1 (4)	-
Tominaga et al 2005	155	1.3 (2)	50.0 (1)
Kurokawa et al 2005	180	1.1 (2)	50.0 (1)
Whitlow et al 1997	59	1.7 (1)	0 (0)
Haggitt et al 1985	64	3.1 (2)	0 (0)
Geraghty et al 1991	81	2.5 (2)	-
Suzuki et al 2003	65	3.1 (2)	100 (2)
Sakuragi et al 2003	278	2.5 (7)	57.1 (4)
Seitz et al 2004	116	3.4 (4)	-
Wang et al 2005	159	4.4 (7)	85.7 (6)
Morson et al 1984	61	5 (3)	-
Cooper et al 1995	140	5.7 (8)	-
Netzer et al 1998	62	8.1 (5)	40.0 (2)
Hackelsberger et al 1995	87	11.5 (10)	-
Hassan et al 2005	380	14.7 (56)	23.2 (13)
Nascimbeni et al 2002	344	34.0 (117)	-
Nascimbeni et al 2004	144	39.6 (57)	-

Table 3. Incidence of G3 Poorly Differentiated T1 Colorectal Carcinoma and Incidence of Nodal Involvement. In those studied with a higher incidence of G3 carcinoma, incidence of nodal disease in those carcinomas falls. From[3]

3.3. Depth of invasion

Haggitt's classification is based on the greatest anatomical depth of invasion in pedunculated polyps.[5] Haggitt 0 lesions are confined to the mucosa. Haggitt grades 1-3 breach the submucosa within the polyp, and they are confined to the head, neck and stalk of the polyp respectively. Only Haggitt 4 lesions invade past the stalk into the submucosa of the wall. Most authors would agree that only Haggitt 4 lesions require further treatment. If adequately excised, Haggitt 0-3 lesions have a risk of recurrence (<1%) which is lower than the predicted mortality of an oncological resection.[15,16] Conversely, for level 4 lesions, Haggitt reported nodal disease rates of almost 13%.

All sessile lesions are Haggitt 4 by definition, but other authors have treated selected sessile lesions with polypectomy alone to good effect. Kudo produced a refinement for sessile polyps by dividing the submucosa into thirds.[13] This has become known as the Kikuchi classification. [2] Lesions confined to the superficial third of the submucosa (called Sm1) demonstrated very low rates of nodal disease and many authors recommend no further

treatment after polypectomy for Sm1. In the absence of other risk factors most would agree for Sm2 lesions as well.[7]

The Kikuchi classification has been widely accepted for the assessment of T1 colorectal tumours but can be difficult to perform on endoscopy specimens as the *muscularis propria* is not usually included in the specimen.[2]

Difficulty is also encountered when the *muscularis mucosa* cannot be identified. A large collaborative Japanese study used Haggitt level 2 (i.e. the border between the head and neck of the polyp) as a baseline for pedunculated polyps. Provided that there was no lymphatic invasion, they found no nodal disease if the depth of invasion from here was <3mm. For sessile polyps the superficial aspect of the lesion was used and again no nodal disease discovered if the invasion was <1mm, regardless of other lymphatic invasion. [17] Other Japanese studies have also found good correlation between quantitative measures of submucosal invasion and risk of lymph node metastasis.[18,19]

Although the study included operative specimens as well as endoscopically removed malignant polyps, Ueno[14] showed that the width of tumour invasion is also an important factor.

3.4. Incomplete or piecemeal resection

Involved resection margins have been shown to be strongly associated with poor outcomes. These patients have higher mortality, local recurrence and rates of residual disease. In one, all be it small, study 75% of incompletely resected polyps were associated with an adverse outcome.[20] It should be noted that even when incomplete resection is reported, absence of residual disease in the surgical specimen is the rule (94% in one study) rather than the exception[21]. This is likely due to diathermy electrofulguration of the remnant.

The European recommendations state that tumour cells within 1mm of the margin represents a positive margin[22], with some authors arguing then >2mm represents the true safe margin[21].

Incomplete removal is failure of primary therapy and requires further resection. Piecemeal removal of the polyp prevents proper histological assessment and surgery is mandated in all cases. For this reason endoscopic mucosal resection by the strip biopsy method is discouraged for the removal of potentially malignant lesions.

3.5. Lymphatic and vascular invasion

Lymphatic invasion has been sighted by some authors as an important predictor of nodal disease. Controversy exists however as reported cases are rare and usually associated with poorly differentiated tumours or incomplete resection. Inter-observer variability and the ease of mistaking retraction artefact for lymphatic invasion also make interpretation difficult.[6,12]

Lymphatic invasion is usually associated with other high risk factors and in those cases with adverse outcomes, almost invariably so. Many authors would regard its status as an independent risk factor is unclear.[20] However a large multi-centre retrospective study from Ja-

pan found lymphatic involvement to be highly significant for nodal metastases (odds ratio 4.69 $P < 0.0001$) in a multivariate analysis of risk factors.[17] They also found that in a small number of cases adverse outcomes were seen from cases of lymphatic invasion, despite invasion being confined to the head of the polyp (Haggit 1).

Vascular invasion is also considered difficult to identify, but where present, it is strongly associated with nodal disease. Yasuda[18] studied T1 rectal tumours, including specimens from primary resections and resections after polypectomy. The odds ratio for the nodal metastasis with reference to the presence or absence of vascular invasion was 12.023 (3.751–116.751 $p = 0.001$). Another study of sessile T1 colorectal carcinomas found that vascular invasion was a significant factor in both univariate and multivariate analysis. However they admit that the small number of cases of vascular invasion were found in lesions with deeper Sm3 invasion.[23]

An odds ratio of 7 (2.6–19.2) for lymph node metastasis was reported in the only meta-analysis looking specifically at malignant polyps and the presence of vascular invasion.[1] However, the same analysis demonstrated no such increased risk in polyps that would otherwise be considered low risk. It may well be that vascular invasion carries no special significance in itself and should not be emphasised in decision making.

3.6. Tumour budding

Tumour budding is the presence of microscopic islands of tumour cells out ahead of the main front of tumour invasion. At present there is no defined agree standard to reporting the phenomenon but several authors have found it to be highly significant. Yasuda reported an odds ratio of 11.11 (3.64–146.03)[18] for predicting nodal disease but until further study occurs it is difficult to make firm recommendations.

3.7. Location

T1 rectal tumours seem to be particularly likely to cause nodal disease, especially when located in the lower third.[15,23] However at this stage there have been no studies looking at this relationship specifically in malignant polyps.

4. “The low risk polyp”

Several authors, starting with Morson in 1984[24], have developed the concept of the low risk polyp. That is, a polyp which can be safely treated with polypectomy alone, as there is minimal risk of nodal disease. The concept has been incorporated into the American College of Gastroenterology guide lines[25]. They recommend no further treatment if:

The polyp is considered to be completely excised by the endoscopist and is submitted *in toto* for pathological examination.

In the pathology laboratory, the polyp is fixed and sectioned so that it is possible to accurately determine the depth of invasion, grade of differentiation, and completeness of excision of the carcinoma.

The cancer is not poorly differentiated.

There is no vascular or lymphatic involvement.

The margin of excision is not involved. Invasion of the stalk of a pedunculated polyp, by itself, is not an unfavourable prognostic finding, as long as the cancer does not extend to the margin of stalk resection.

The European recommendations, while noting the potential of tumour budding and lymphatic and vascular invasion as prognostic factors, decline to provide a guideline as they have not been statistically significant in all cases.[22]

Another perspective is given by Nicholls,[7] who instead offered an algorithmic approach. He differentiates between colonic and rectal polyps. For rectal lesions judged to be adenoma prior to resection he recommends that all poorly differentiated lesions be removed. For colonic polyps he suggested further resection solely for Haggitt 4 polyps (including by definition all sessile polyps) with a depth of invasion >1000 μm .

Systematic review of studies which selected low risk polyps using methodology broadly similar to the American criteria has demonstrated very low rates of nodal recurrence. (See Table 4). Mortality from oncological resection varies greatly by age and co-morbidity but is usually quoted around 3-5%.[26-28] Therefore, for these lesions, the safest course of action is surveillance rather than further resection.[8,29]

It should be noted that these criteria take no account of the depth of invasion and that these guidelines would encourage the removal of some lesions that have been safely treated by endoscopy. It may be that they are documenting many of the same characteristics but in a different way. It is not hard to imagine that Sm3 lesions are less likely to be excised with clear margins and are more likely to show poor differentiation. Indeed a large study of surgically resected sessile T1 colorectal tumours found Sm3 invasion in 68% of G3+4 tumours and on 33% in G1+2 ($P=0.001$). This study also found tumour grade not to be significant on multivariate analysis.[23]

Given Japanese experience it maybe be better to refine the criteria for a low risk polyp as any polyp lacking all of these features:

High grade (G3-4) lesions.

Incomplete resection or other factors preventing adequate histological assessment of the lesion.

Piecemeal resection

Depth of invasion greater than 2mm from *muscularis mucosa*

Width of invasion greater than 4mm.

The utility of including lymphatic invasion, vascular invasion or tumour budding is unclear at this time. Further work should be done to examine the risk from polyps of the lower third of the rectum, especially as these can often require a permanent stoma if oncological resection is performed.

Study	No. Of Polyps	Unfavourable Outcome	Unfavourable outcome in low risk group
Bernard et al. 1988	19	3	0
Christie 1988	88	6	0
Conte et al. 1987	30	4	0
Cooper et al. 1995	140	16	0
Cranley et al. 1986	39	10	0
Cunningham et al. 1994	36	2	0
Eckardt et al. 1988	61	11	0
Fried et al. 1984	22	0	0
Geraghty et al. 1991	80	5	0
Hackelsberger et al. 1995	86	8	0
Kikuchi et al. 1995	78	9	0
Kyzer et al. 1992	42	1	0
Morson et al. 1984	60	2	0
Netzer et al. 1998	70	16	0
Rossini et al. 1988	66	4	0
Shatney et al. 1975	28	1	0
Speroni et al. 1988	30	2	0
Sugihara et al. 1989	25	3	0
Volk et al. 1995	47	10	0
Whitlow et al. 1997	59	4	0
Seitz et al. 2004	114	16	0
Total	1,227	135	0

Table 4. Incidence of Adverse Outcome in Low Risk Polyps. Low risk = excision complete with resection margins of at least 2 mm, no Grade 3 carcinoma, and no vascular invasion. (From Sitz et al. 2004)

5. “The high risk polyp”

Polyps that do not meet the low risk criteria should be considered for surgical removal even if there has been total excision of the primary lesion. Indeed, it is unusual to find residual tumour in the surgical specimen, especially if the lesion had clear histological margins.[6] The justification for surgery is the desire for regional control as the risk of nodal disease is much higher in these patients and oncological resection is required to obtain regional control in a similar manner to other colorectal malignancies. The dilemma is that only a minority of these patients have nodal disease requiring control and these patients are only reliably identified after resection. Especially in elderly, the decision to resect has the possibility to cause considerable harm without producing a benefit to the patient.

5.1. “First do no harm...”

It is an old surgical adage that surgery is only indicated if the natural history of the cure is better than the natural history of the disease. In situations of uncertainly like this it is useful to examine the possible outcomes of proposed courses of action in order to see were the survival advantage lies.

The outcomes of the decision to operate will be a function of the risk of nodal disease and the risk of operative mortality and morbidity. We feel it is useful to consider these decisions with reference to a 2x2 table of results

		Nodal disease	
		Yes	No
Further Resection	Yes	Survival similar to resected Stage IIIa disease (roughly 75%)	Operative mortality (Variable)
	No	Survival as for stage IV disease (Roughly 5%)	Curative procedure, without operative mortality (Roughly 100%)

Table 5. 2x2 Table of outcomes from the decision regarding further resection of high risk malignant polyps.

5.2. Nodal disease and oncological resection

We see no reason to regard these patients as any different from patients who had proceeded straight to oncological resection and post operatively were staged either IIIa to IIIc (TNM v5). In the SEER data from 1998 to 2000 there is a huge difference between those with regard to five year survival (73% vs. 28% respectively). Clearly this stage differentiation has huge implications for the advisability of surgery. It has been suggested that T1-2N2 tumours have a better survival than T3-4N2 tumours and the TNMv6 classification has been changed to reflect this. Newer SEER data shows five year survival of 87.7% for T1-2N1 disease and 75% for T1-2N2 disease. [30]

To our knowledge there is no current method of estimating the extent of nodal disease from polypectomy histology.

5.3. Nodal disease and no further resection

For those patients with nodal disease who do not have it resected the prognosis is likely to be compromised. Intensive surveillance is likely to detect continued disease progression.

The role of chemotherapy and or radiotherapy has not been clearly defined in this group but is likely to be palliative in nature.

5.4. Absence of Nodal disease

The survival of patients after endoscopic removal of T1 lesions and no nodal disease is excellent. The mortality in these groups will be limited to the operative mortality from further resection.

5.5. Risk of Nodal disease

Various figures have been quoted in the text for the risk of nodal disease in high risk patients. This can partly be explained by the differing criteria used to define risk by various authors. Further stratification within the “high risk group” may become apparent with further study.

The St Mark’s Lymph Node Positivity Model[31] can be used to predict the individual risk of nodal metastasis after local resection of rectal tumours. However it makes no distinction within T1 tumours. Such assessment of individual risk factors to produce a personalised risk is not possible based on the current evidence. Further studies using multivariate analysis will be required to tease out the importance of individual risk factors.

For our analysis we have chosen to present data based on Sm depth as this has shown to be a reproducible predictor of nodal disease. Both Kikuchi and Nascimbeni reported rates of roughly 5, 10 and 25% for Sm 1, 2 and 3 respectively.[23,32]

Risk Factor	Incidence of nodal disease
Depth of invasion	Haggit 1.2.3 = <1%[9] Kikuchi SM1 = 5% Kikuchi Sm2 = 10% Kicuchi Sm3 = 25%[23, 32]
Poorly differentiated	25-100%. <i>Not found to be important in multivariate analysis.</i> [14, 17]
Lympho-vascular Invasion	41% <i>Poor reproducibility.</i> [18]
Incomplete resection	75%[20]

Table 6. Incidence of nodal disease by risk factor

5.6. The risk of further resection

Oncological resection of colorectal lesions is performed via segmental resection of the affected portion of the bowel and its draining lymph node basin. Harvesting these nodes gains local control and definitively stages the disease. It is a major undertaking with considerable risks. In the case of very low rectal tumours an abdomino-perineal excision of rectum (APER) results in permanent stoma formation.

In the UK at least, operative mortality has fallen in recent years. 30 day mortality was 6.8% in 1999, falling to 3.7% in 2009/10.[33,34] Rates from Scandinavia (4.8%)[26] and the US (3.1%)[27] are broadly similar. This remains considerably higher than the rate of nodal disease in the low risk malignant polyps. The 90 day mortality rate, considered by some authors to be a more accurate measure of operative mortality is higher still, is 5.6% in the UK.[34]

This baseline rate is affected by both tumour and patient factors. Patients over the age of 80 are over ten times more likely to die than those under 50 (15% vs 1.2% 30 day mortality). [28,33] Comparing ASA1 and ASA4 patients, the odds ratio for death at 30 days is 14.06. Patients with rectal tumours do better than those with colonic tumours, though this seems to be due to high mortality for patients undergoing subtotal or total colectomy. Female sex, affluence, high volume surgical centres and elective rather than emergency surgery all also have a beneficial effect.[33]

On top of mortality, anastomotic leaks, wound complications, cardiovascular complications, defecatory disorders and the psychological impact of stoma formation must also be considered when deciding whether or not to resect. Morbidity rates of up to 35% have been reported in the past.[15] These seem to affect laparoscopic surgery as much as open resections, but hospital discharge and return to work occurs sooner following laparoscopic procedures. [35,36]

A more accurate individualised operative risk can be estimated from risk scoring systems. CR-POSSUM uses patient and operative parameters to estimate operative risk on an individual basis and has been well validated.[37,38] Cardiopulmonary exercise testing is also useful in predicting complications and the length of hospital stay. Both these tools can be of great use to the surgeon and patient when used thoughtfully during surgical planning. [39]

5.7. The special case of rectal tumours

There has been considerable interest in recent years in local resection of early rectal tumours to avoid stoma formation. This is relevant as malignant polyps in the rectum are a variety of early rectal tumour. Transanal Endoscopic Microsurgery (TEMs) allows full thickness excision of rectal lesions below the peritoneal fold, with excellent rates of local recurrence.[15] Its ability to harvest local lymph nodes is limited, and as such it is not generally a suitable second procedure for high risk lesions. It may have a role as secondary procedure for incompletely removed polyps which otherwise show favourable features. In its guidance the ACPGBI recommended full classical resection of rectal tumours that show the high risk features described earlier.[40]

The anatomical location of the draining nodes in rectal lesions has also encouraged more extensive use of imaging to predict local nodal metastases. Endoanal Ultrasound and MRI both have the ability to detect enlarged local nodes; however distinguishing between the commonly found reactive nodes and metastases can be difficult. Micrometastases have also been detected in radiologically normal nodes. The use of new contrast agents may improve accuracy but currently histological examination remains the gold standard for detecting nodal disease. [15]

For locally excised T1 and T2 tumours adjuvant chemoradiotherapy has been used with success to prevent local recurrence if further surgery is not deemed appropriate. The role of adjuvant therapy in malignant polyps is unexplored at this time.

5.8. Calculating the survival advantage

As the nodal status of these patients is unknown prior to surgery, mortality is a composite of the mortality of those with and without nodal disease. The contribution from each group will be in proportion to the risk of nodal disease.

$$cM = R.NM + (1-R).nM$$

Where cM= Composite mortality

R =Risk of nodal disease

NM =Mortality of those with nodal disease

nM =Mortality of those without nodal disease

The best course of action can be discerned by calculating the difference between cM with and without surgery. Tables 7-9 contain sample composite survival figures and number needed to treat at five years for various stages of malignant polyp.

Using this method we can see that for a patient with a Sm3 lesion (25% of nodal disease) and a predicted operative mortality of 2% there will be an absolute risk reduction of mortality at 5 years of 16% (NNT 6.25) if 5 year survival of node positive patients is 75% and a 4.5% reduction (NNT 21.05) if 5 year survival of node positive patients is 27%. In stage IIIa (75% five year survival) disease the absolute risk is reduced by 10% (NNT 1), but this disappears for stage IIIc. There has been considerable debate regarding the need to resect Sm2 lesions. In this model the benefit from resection disappears once operative mortality reaches 5% for IIIa lesions and 10% for IIIc lesions. Clearly careful though needs to be given to risk when choosing to operate on these patients.

Obviously this model makes no account of operative morbidity. For patients with IIIc disease and Sm3 lesions there is a survival advantage to operating; however the decision to subject 40 patients to major surgery to save 1 life at five years needs careful consideration.

	Patient A	Patient B	Patient C	Patient D
Age	55	55	80	60
Lesion	Kikuchi Sm3	Haggit level 1	Kikuchi Sm2	Kikuchi Sm1
Risk of nodal disease	25%	<1%	10%	5%
Operative Mortality	1%	1%	10%	5%
Compsite Survival without further resection	81.00	"/>99%	90.50	95.25
Compsite survival with resection	94.20	99%	88.50	94.00
Survival advantage	13.20	-	-	-

Table 7. Examples of using composite survival to inform decision making in patients with malignant polyps

6. Conclusion

This problem has been known and debated for over 30 years.[41] As the role of endoscopy has grown and developed, guidelines have been formulated to help clinicians make beneficial choices. Unfortunately the small scale and heterogeneity for published work had prevented any guidelines from gaining universal acceptance. The focus on tumour grade in the American guidance has been challenged by work from Japan that emphasises the importance of quantitative measures of the depth of invasion. Japanese work has also shown lymphatic invasion, vascular invasion and tumour budding to be of high prognostic significance, but concerns about reproducibility have prevented their universal adoption. It is also unclear which observed prognostic factors are truly significant and which are confounding. None of the prognostic factors identified are highly specific and clinicians must still make difficult decisions based on the balance of risk.

The solution to this problem will surely come from improved pre-operative staging. Endo-anal ultra sound and targeted contrast MRI have both shown promise for rectal tumours. Sentinel node mapping in the colon has also been investigated but remains experimental. [42]

Until highly accurate pre-operative staging of nodal disease is possible effort must be made to refine the classification of malignant polyps to identify the truly significant prognostic factors. It is the opinion of the authors that an individualised prediction model comparing operative surgical risk and risk of progressive disease should be used to counsel patients regarding future strategies. Creation of a national or international database would facilitate better predictive models.

Risk Of Nodal Disease/%		Operative Survival/ %				
		99	98	95	90	85
5	No Resectio /%	95.25	95.25	95.25	95.25	95.25
	Resection/%	98.45	97.50	94.65	89.90	85.15
	Survival Advantage/%	3.20	2.25	-	-	-
	NNT	31.25	44.44	-	-	-
10	No Resection/%	90.50	90.50	90.50	90.50	90.50
	Resection/%	97.90	97.00	94.30	89.80	85.30
	Survival Advantage/%	7.40	6.50	3.80	-	-
	NNT	13.51	15.38	26.32	-	-
15	No Resection/%	85.75	85.75	85.75	85.75	85.75
	Resection/%	97.35	96.50	93.95	89.70	85.45
	Survival Advantage/%	11.60	10.75	8.20	3.95	-
	NNT	8.62	9.30	12.20	25.32	-
20	No Resection/%	81.00	81.00	81.00	81.00	81.00
	Resection/%	96.80	96.00	93.60	89.60	84.00
	Survival Advantage/%	15.80	15.00	12.60	8.60	3.00
	NNT	6.33	6.67	7.94	11.63	33.33
25	No Resection/%	76.25	76.25	76.25	76.25	76.25
	Resection/%	96.25	95.50	93.25	89.50	85.75
	Survival Advantage/%	20.00	19.25	17.00	13.25	9.50
	NNT	5.00	5.19	5.88	7.55	10.53
30	No Resection/%	71.50	71.50	71.50	71.50	71.50
	Resection/%	95.70	95.00	92.90	89.40	85.90
	Survival Advantage/%	24.20	23.50	21.40	17.90	14.40
	NNT	0.04	0.04	0.05	0.06	0.07

Table 8. 5 year survival, survival advantage with further resection and number needed to treat if 5 year survival for node positive patients is 88% after resection.

Risk Of Nodal Disease/%		Operative Survival/ %				
		99	98	95	90	85
5	No Resection/%	95.25	95.25	95.25	95.25	95.25
	Resection/%	97.80	96.85	94.00	89.25	84.50
	Survival Advantage/%	2.55	1.60	-	-	-
	NNT	39.22	62.50	-	-	-
10	No Resection/%	90.50	90.50	90.50	90.50	90.50
	Resection/%	96.60	95.70	93.00	88.50	84.00
	Survival Advantage/%	6.10	5.20	2.50	-	-
	NNT	16.39	19.23	40.00	-	-
15	No Resection/%	85.75	85.75	85.75	85.75	85.75
	Resection/%	95.40	94.55	92.00	87.75	83.50
	Survival Advantage/%	9.65	8.80	6.25	2.00	-
	NNT	10.36	11.36	16.00	50.00	-
20	No Resection/%	81.00	81.00	81.00	81.00	81.00
	Resection/%	94.20	93.40	91.00	87.00	83.00
	Survival Advantage/%	13.20	12.40	10.00	6.00	2.00
	NNT	7.58	8.06	10.00	16.67	50.00
25	No Resection/%	76.25	76.25	76.25	76.25	76.25
	Resection/%	93.00	92.25	90.00	86.25	82.50
	Survival Advantage/%	16.75	16.00	13.75	10.00	6.25
	NNT	5.97	6.25	7.27	10.00	16.00
30	No Resection/%	71.50	71.50	71.50	71.50	71.50
	Resection/%	91.80	91.10	89.00	85.50	82.00
	Survival Advantage/%	20.30	19.60	17.50	14.00	10.50
	NNT	4.93	5.10	5.71	7.14	9.52

Table 9. 5 year survival, survival advantage with further resection and number needed to treat if 5 year survival is 75% after resection.

Risk Of Nodal Disease/%		Operative Survival/ %				
		99	98	95	90	85
5	No Resection/%	95.25	95.25	95.25	95.25	95.25
	Resection/%	95.30	94.35	91.50	86.75	82.00
	Survival Advantage/%	0.05	-	-	-	-
	NNT	2000.00	-	-	-	-
10	No Resection/%	90.50	90.50	90.50	90.50	90.50
	Resection/%	91.60	90.70	88.00	83.50	79.00
	Survival Advantage/%	1.10	0.20	-	-	-
	NNT	90.91	500.00	-	-	-
15	No Resection/%	85.75	85.75	85.75	85.75	85.75
	Resection/%	87.90	87.05	84.50	80.25	76.00
	Survival Advantage/%	2.15	1.30	-	-	-
	NNT	46.51	76.92	-	-	-
20	No Resection/%	81.00	81.00	81.00	81.00	81.00
	Resection/%	84.20	83.40	81.00	77.00	73.00
	Survival Advantage/%	3.20	2.40	0.00	-	-
	NNT	31.25	41.67	-	-	-
25	No Resection/%	76.25	76.25	76.25	76.25	76.25
	Resection/%	80.50	79.75	77.50	73.75	70.00
	Survival Advantage/%	4.25	3.50	1.25	-	-
	NNT	23.53	28.57	80.00	-	-
30	No Resection/%	71.50	71.50	71.50	71.50	71.50
	Resection/%	76.80	76.10	74.00	70.50	67.00
	Survival Advantage/%	5.30	4.60	2.50	-	-
	NNT	18.87	21.74	40.00	-	-

Table 10. 5 year survival, survival advantage with further resection and number needed to treat if 5 year survival in node positive patients is 27% after resection.

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References

- [1] Hassan C, Zullo A, Risio M, Rossini FP, Morini S. Histologic risk factors and clinical outcome in colorectal malignant polyp: a pooled-data analysis. *Dis Colon Rectum* 2005;48 1588-1596.
- [2] Bujanda L, Cosme A, Gil I, Arenas-Mirave JI. Malignant colorectal polyps. *World J Gastroenterol* 2010;16 3103-3111.
- [3] Ueno H, Hashiguchi Y, Kajiwara Y, Shinto E, Shimazaki H, et al. Proposed objective criteria for "grade 3" in early invasive colorectal cancer. *Am J Clin Pathol* 2010;134 312-322.
- [4] Risio M. The Natural History of pT1 Colorectal Cancer. *Front Oncol* 2012;2 22.
- [5] Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. *Gastroenterology* 1985;89 328-336.
- [6] Mitchell PJ, Haboubi NY. The malignant adenoma: when to operate and when to watch. *Surg Endosc* 2008;22 1563-1569.
- [7] Nicholls RJ, Zinicola R, Binda GA. Indications for colorectal resection for adenoma before and after polypectomy. *Tech Coloproctol* 2004;8 Suppl 2 s291-294.
- [8] Volk EE, Goldblum JR, Petras RE, Carey WD, Fazio VW. Management and outcome of patients with invasive carcinoma arising in colorectal polyps. *Gastroenterology* 1995;109 1801-1807.
- [9] Seitz U, Bohnacker S, Seewald S, Thonke F, Brand B, et al. Is endoscopic polypectomy an adequate therapy for malignant colorectal adenomas? Presentation of 114 patients and review of the literature. *Dis Colon Rectum* 2004;47 1789-1796; discussion 1796-1787.
- [10] Cooper HS, Deppisch LM, Gourley WK, Kahn EI, Lev R, et al. Endoscopically removed malignant colorectal polyps: clinicopathologic correlations. *Gastroenterology* 1995;108 1657-1665.
- [11] Coverlizza S, Risio M, Ferrari A, Fenoglio-Preiser CM, Rossini FP. Colorectal adenomas containing invasive carcinoma. Pathologic assessment of lymph node metastatic potential. *Cancer* 1989;64 1937-1947.
- [12] Geraghty JM, Williams CB, Talbot IC. Malignant colorectal polyps: venous invasion and successful treatment by endoscopic polypectomy. *Gut* 1991;32 774-778.
- [13] The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. *Gastrointest Endosc* 2003;58 S3-43.

- [14] Ueno H, Mochizuki H, Hashiguchi Y, Shimazaki H, Aida S, et al. Risk factors for an adverse outcome in early invasive colorectal carcinoma. *Gastroenterology* 2004;127:385-394.
- [15] Tytherleigh MG, Warren BF, Mortensen NJ. Management of early rectal cancer. *Br J Surg* 2008;95:409-423.
- [16] Kyzer S, Begin LR, Gordon PH, Mitmaker B. The care of patients with colorectal polyps that contain invasive adenocarcinoma. Endoscopic polypectomy or colectomy? *Cancer* 1992;70:2044-2050.
- [17] Kitajima K, Fujimori T, Fujii S, Takeda J, Ohkura Y, et al. Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study. *J Gastroenterol* 2004;39:534-543.
- [18] Yasuda K, Inomata M, Shiromizu A, Shiraiishi N, Higashi H, et al. Risk factors for occult lymph node metastasis of colorectal cancer invading the submucosa and indications for endoscopic mucosal resection. *Dis Colon Rectum* 2007;50:1370-1376.
- [19] Sakuragi M, Togashi K, Konishi F, Koinuma K, Kawamura Y, et al. Predictive factors for lymph node metastasis in T1 stage colorectal carcinomas. *Dis Colon Rectum* 2003;46:1626-1632.
- [20] Netzer P, Forster C, Biral R, Ruchti C, Neuweiler J, et al. Risk factor assessment of endoscopically removed malignant colorectal polyps. *Gut* 1998;43:669-674.
- [21] Jang EJ, Kim DD, Cho CH. Value and interpretation of resection margin after a colonoscopic polypectomy for malignant polyps. *J Korean Soc Coloproctol* 2011;27:194-201.
- [22] Quirke P, Risio M, Lambert R, von Karsa L, Vieth M. Quality assurance in pathology in colorectal cancer screening and diagnosis-European recommendations. *Virchows Arch* 2011;458:1-19.
- [23] Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. *Dis Colon Rectum* 2002;45:200-206.
- [24] Morson BC, Whiteway JE, Jones EA, Macrae FA, Williams CB. Histopathology and prognosis of malignant colorectal polyps treated by endoscopic polypectomy. *Gut* 1984;25:437-444.
- [25] Bond JH. Polyp guideline: diagnosis, treatment, and surveillance for patients with colorectal polyps. Practice Parameters Committee of the American College of Gastroenterology. *Am J Gastroenterol* 2000;95:3053-3063.
- [26] Frederiksen BL, Osler M, Harling H, Ladelund S, Jorgensen T. The impact of socioeconomic factors on 30-day mortality following elective colorectal cancer surgery: a nationwide study. *Eur J Cancer* 2009;45:1248-1256.
- [27] Dimick JB, Cowan JA, Upchurch GR, Colletti LM. Hospital volume and surgical outcomes for elderly patients with colorectal cancer in the United States¹ Presented at

the Annual Meeting of the Association for Academic Surgery, Boston, MA, November 7th–9th, 2002. *The Journal of surgical research* 2003;114 50-56.

- [28] Latkauskas T, Rudinskaite G, Kurtinaitis J, Janciauskiene R, Tamelis A, et al. The impact of age on post-operative outcomes of colorectal cancer patients undergoing surgical treatment. *BMC Cancer* 2005;5 153.
- [29] Ruiz-Tovar J, Jimenez-Miramón J, Valle A, Limones M. Endoscopic resection as unique treatment for early colorectal cancer. *Rev Esp Enferm Dig* 2010;102 435-441.
- [30] Gunderson LL, Jessup JM, Sargent DJ, Greene FL, Stewart AK. Revised TN categorization for colon cancer based on national survival outcomes data. *J Clin Oncol* 2010;28 264-271.
- [31] Risk Prediction in Surgery. <http://www.riskprediction.org.uk/> (Accessed 1st August 2012)
- [32] Kikuchi R, Takano M, Takagi K, Fujimoto N, Nozaki R, et al. Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. *Dis Colon Rectum* 1995;38 1286-1295.
- [33] Morris EJ, Taylor EF, Thomas JD, Quirke P, Finan PJ, et al. Thirty-day postoperative mortality after colorectal cancer surgery in England. *Gut* 2011;60 806-813.
- [34] National Bowel Cancer Audit Report 2011. http://www.ic.nhs.uk/webfiles/Services/NCASP/audits%20and%20reports/Bowel_Cancer_Audit_Report_2011_interactive.pdf (Accessed 1st August 2012)
- [35] Leung KL, Kwok SP, Lam SC, Lee JF, Yiu RY, et al. Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. *Lancet* 2004;363 1187-1192.
- [36] Lourenco T, Murray A, Grant A, McKinley A, Krukowski Z, et al. Laparoscopic surgery for colorectal cancer: safe and effective? - A systematic review. *Surg Endosc* 2008;22 1146-1160.
- [37] Al-Homoud S, Purkayastha S, Aziz O, Smith JJ, Thompson MD, et al. Evaluating operative risk in colorectal cancer surgery: ASA and POSSUM-based predictive models. *Surg Oncol* 2004;13 83-92.
- [38] Bromage SJ, Cunliffe WJ. Validation of the CR-POSSUM risk-adjusted scoring system for major colorectal cancer surgery in a single center. *Dis Colon Rectum* 2007;50 192-196.
- [39] Struthers R, Erasmus P, Holmes K, Warman P, Collingwood A, et al. Assessing fitness for surgery: a comparison of questionnaire, incremental shuttle walk, and cardiopulmonary exercise testing in general surgical patients. *Br J Anaesth* 2008;101 774-780.
- [40] ASGBI Guidelines for the Management of Colorectal Cancer 3rd Edition. www.acpgbi.org.uk/assets/documents/COLO_guides.pdf (Accessed 1st August 2012)

- [41] Morson BC, Bussey HJ, Samoorian S. Policy of local excision for early cancer of the colorectum. *Gut* 1977;18 1045-1050.
- [42] Cahill RA, Leroy J, Marescaux J. Could lymphatic mapping and sentinel node biopsy provide oncological providence for local resectional techniques for colon cancer? A review of the literature. *BMC Surg* 2008;8 17.

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