Review Article (Current Strategies in Colon Cancer Management)

# Management of malignant colonic polyps

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**Abstract:** With the implementation of colorectal cancer screening programs, there has been an increasing incidence of malignant colonic polyps (MP). The attending surgeon is often faced with the management dilemma of whether polypectomy can be considered adequate treatment or if formal oncological resection is required. While endoscopic therapy avoids the risks and morbidity of surgery, there is a potential trade-off of under-staging and inadequate treatment. Surgery, on the other hand confers the benefits of clear resection margins, nodal staging and the ability to prognosticate and guide the decision for adjuvant therapy. This article sets out to review the histopathologic prognostic factors of MP and the various management and surveillance strategies.

**Keywords:** Malignant colonic polyps (MP); colon cancer; T1 colon cancer

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## Introduction

Malignant colonic polyps (MP) are defined as sessile or pedunculated polyps that harbour cancer cells which have invaded past the muscularis mucosae into the submucosa without crossing the submucosa, regardless of lymph node involvement (1). With the implementation of colorectal cancer screening programs and the increasing availability of colonoscopy, the incidence of MP has increased (2). The prevalence of MP in endoscopically removed polyps has been reported to be between 0.75% and 5.6% (3).

Endoscopic removal of these polyps can be achieved by conventional snare polypectomy or advanced endoscopic methods such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) depending on the nature of the polyp and availability of expertise (4).

After a diagnosis of MP is made, the subsequent management is often contentious because the rate of remnant cancer cells in the bowel wall and regional lymph nodes vary amongst patients. Furthermore, some polyps are removed piecemeal limiting a comprehensive histological analysis of the resection margin. As a result of these variable factors, the attending surgeon is often faced with the conundrum of choosing between major oncological resection versus polypectomy alone. Major surgery though associated with morbidity and mortality, confers the benefits of clear margins, nodal harvest and allows for comprehensive disease staging which will guide the recommendation for adjuvant chemotherapy. Polypectomy saves the patient major surgery, but the issue of under-treatment with risks of recurrent and or metastatic disease remains.

Current practices are guided by the National Clinical Practice Guidelines in Oncology (NCCN) (5) and The Association of Coloproctology of Great Britain and Ireland (ACPGBI) position statement (3). This review article sets out to review the histopathologic prognostic factors of MP and the various management strategies.

## Endoscopic evaluation

The management of MP begins at the index colonoscopy

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**Table 1** Haggitt levels for pedunculated MP

| Haggitt level | Description of depth of invasion of cancer cells |
|---|---|
| 0 | Limited to the mucosa |
| 1 | Into the submucosa but limited to the head of the polyp |
| 2 | Into the level of the neck (junction of the head and the stalk) |
| 3 | Into any part of the stalk |
| 4 | Into the submucosa of the bowel wall below the level of the stalk but above the muscularis propria |

MP, malignant colonic polyps.

**Table 2** Kikuchi classification for sessile MP

| Kikuchi level | Description of depth of invasion of cancer cells |
|---|---|
| SM1 | Upper third of the submucosa |
| SM2 | Middle third of the submucosa |
| SM3 | Lower third of the submucosa |

MP, malignant colonic polyps.

when a diagnosis of MP is suspected. Apart from assessing the size and shape of the polyp, the endoscopist should also evaluate its surface using the Narrow Band Imaging International Colorectal Endoscopic (NICE) (6) or Kudo (7) Classification as a guide and decide if endoscopic resection is suitable.

Sessile polyps that are NICE Type 3 or Kudo Type $V_n$ are worrisome for deep submucosal invasion and should be considered for surgical resection instead. Pedunculated polyps on the other hand are more likely to be amenable to endoscopic resection (4). Suspected MP that are not suitable for endoscopic removal should be biopsied and their locations tattooed to facilitate subsequent surgery (3).

If not suitable for conventional snare polypectomy, the endoscopist can also consider the use of advanced endoscopic techniques such as EMR or ESD for *en bloc* removal of the polyp (4). Following endoscopic removal, the polypectomy site should also be tattooed to aid endoscopic re-evaluation; surgical resection (if required) and surveillance (3).

After endoscopic removal of the polyp, the patient should be assessed for risk of remnant disease and lymph node metastasis based on the following factors to determine if surgery is required or has polypectomy been adequate treatment.

## Depth of invasion

The Haggitt classification is routinely used to describe the level of invasion of cancer cells in pedunculated MP and is summarized in *Table 1* (8). For sessile MP, Kudo and Kikuchi described a separate classification system based on the depth of invasion into the submucosa (*Table 2*) (9,10). These classification systems help prognosticate and guide subsequent therapy for MP.

The Kikuchi classification can however be difficult to ascertain in cases where the histological specimen does not contain muscularis propria. This issue has been addressed by Kitajima *et al.* who described the technique of measuring the depth of submucosal invasion by cancer cells from the level of the muscularis mucosa (11).

Numerous studies demonstrate that a deeper depth of invasion is related to increased lymph node metastasis and a poorer outcome (8,10,11). Haggitt reported in 1985 that a depth of invasion to Haggitt level 4 is a significant adverse prognostic factor for pedunculated MP (8). Likewise, Nitvatvongs showed that for pedunculated MP with Haggitt levels 1 to 3, there was no incidence of lymph node metastasis but for level 4 lesions, the risk of lymph node metastasis was as high as 27% (12). Kikuchi reported that for sessile MP, the risk of lymph node metastasis was as low as 0% in SM1 lesions but increased to 14.4% in SM3 lesions (10). In 2004, Kitajima demonstrated that for sessile MP, the risk of lymph node metastasis was 0% if the depth of submucosal invasion was less than 1,000 μm but increased to more than 11.5% when the depth of invasion exceeded 1,000 μm (10). In a meta-analysis by Beaton *et al.*, the authors also reported that the risk of lymph node metastasis was significantly higher when the depth of submucosal invasion was more than 1,000 μm (OR 3.87, 95% CI: 1.50–10.00, P=0.005) (13).

As such, surgical resection is recommended for pedunculated MP which are Haggitt level 4. For sessile MP, surgery is recommended for SM3 lesions and those with a submucosal invasion of more than 1,000 μm.

More recently, there is some evidence to show that in addition to the depth of invasion, the width and area of submucosal invasion is also a significant predictor for lymph node metastasis. Toh reported that a width of invasion more than 11.5 mm and an area of submucosal invasion more than 35 $mm^2$ were significant predictors for lymph node metastasis (14). This study was however limited by its retrospective nature and small sample size. When more concrete data is available, these two factors may eventually impact the decision for surgery.

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**Table 3** Histological grade for colon and rectum cancer

| Grade | Description of depth of invasion of cancer cells |
|---|---|
| Low | Well and moderately differentiated, greater than or equal to 50% gland formation |
| High | Poorly differentiated and undifferentiated, less than 50% gland formation |

## Lymphovascular invasion (LVI)

LVI is defined by the presence of tumour cells within an endothelial-lined channel (15). Kitajima and Okabe both demonstrated that LVI is a significant independent risk factor for lymph node metastasis (11,16). Hassan conducted a pooled-data analysis of 1,900 patients with MP and found that LVI was present in 17.6% of MP. LVI was also found to be more common in sessile MP as compared to pedunculated MP. The authors found that the rate of lymph node metastasis was significantly higher in MP with LVI than those without (35.3% *vs.* 7.2%, OR 7, 95% CI: 2.6–19.2). However, they did not find any significant difference in terms of residual cancer in the bowel wall, hematogenous metastasis, or mortality between the 2 groups (17). Similarly, in a meta-analysis by Beaton et al, LVI was also shown to be significantly associated with nodal involvement (OR 4.81, 95% CI: 3.14–7.37, P<0.00001) (13).

LVI is significantly associated with lymph node metastasis in MP and surgical resection is recommended.

## Histological grade

There are several histological grading systems for colorectal cancer, but a single widely accepted standard is lacking (18). Furthermore, there is also significant interobserver variability amongst pathologists (3). As such the College of American Pathologists Consensus recommends a 2-tiered grading system (*Table 3*). By doing so, they aim to reduce the interobserver variability between pathologists and improve the prognostic significance of each grade (19).

In a pooled-data analysis by Hassan, poor differentiation was described in 7.2% and was more common in sessile MP (11.7% *vs.* 6.8%; P=0.05). A poor differentiation was also associated with a higher risk of lymph node metastasis (OR 3.9, 95% CI: 1.9–8.4), hematogenous metastasis (OR 3.9, 95% CI: 2–7.9) and cancer related mortality (OR 9.2, 95% CI: 4.7–18.3) (17). Likewise, Beaton reported in a meta-analysis of 13 studies that when compared to low grade tumours, high grade tumours had a higher risk of lymph node metastasis (OR 5.60, 95% CI: 2.9–10.8, P<0.00001) (13).

High grade MP are associated with a higher risk of lymph node metastasis and poorer oncological outcome and surgical resection is recommended.

## Margin of resection

There is currently no consensus to the definition of a positive margin of resection (5). A positive margin has been defined as (I) tumour less than 1 mm from transected margin; (II) tumour less than 2 mm from transected margin; and (III) tumour cells within the diathermy of the transected margin (5). The Royal College of Pathologists defines a positive margin as tumour extending to ≤1 mm of the resected margin (20,21).

The literature is replete with evidence to show that if tumour cells is at or near the resection margin, there is increased adverse oncological outcomes (17,22,23,24). Hassan reported in a pooled analysis of 20 studies that the resection margin was positive in 33.2% and in these cases there was a higher residual and recurrent disease rate. (26.4% *vs.* 1.6%, OR 22, 95% CI: 10.3–46.6, P<0.0001). The patients with a positive resection margin also had a significantly higher rate of hematogenous metastasis and cancer related mortality (17). Similarly, Cooper described an increased rate of recurrence of up to 33% when the resection margin is ≤1 mm (23). Although there is some evidence to suggest that further treatment is only necessary when tumour is present at the true margin in the absence of other adverse histopathological features (25), it is not sufficiently strong to change the current recommendation of ≤1 mm as margin involvement (20,21).

A deep resection margin of ≤1 mm is associated with adverse oncological outcomes and surgical resection is recommended.

## Tumour budding

Tumour budding is defined as a single tumour cell or a cell cluster of up to 4 tumour cells at the advancing edge of the tumour (26). Numerous studies have demonstrated an association between tumour budding and lymph node metastasis and other adverse oncological outcomes (11,22,27). In a meta-analysis of 7 studies, Beaton found that tumour budding was associated with a higher risk of lymph node metastasis (OR 7.74, 95% CI: 4.47–13.39, P<0.001) (13).

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Presence of tumour budding is associated with an increased risk of lymph node metastasis and surgical resection should be considered.

## Histological tumour type

MP with cribriform or micropapillary variants are associated with a higher risk of lymph node metastasis (28,29). In addition, mucinous or signet ring cell adenocarcinomas are also associated with a poorer prognosis and hence surgical resection is recommended (3,30).

## Other factors

MP which are removed piecemeal often hamper accurate assessment of the resection margin and in these cases, it is prudent to offer surgical resection (3,5).

There is no consensus on the recommended imaging for staging MP. We do a staging computed tomography (CT) scan of the chest, abdomen and pelvis as a baseline at diagnosis as recommended by the ACPGBI position statement (3). If the CT shows suspicious features for lymph node metastasis, surgery is also recommended. Suspicious CT features include size >1 cm, round shape, hilar thinning, calcification, central necrosis, internal heterogeneity, irregular border or perinodal infiltration (31). The sensitivity and specificity for detecting nodal disease is however only 70% (95% CI: 63–73%) and 78% (95% CI: 73–82%) respectively as shown in a meta-analysis by Dighe *et al.* (32).

## Surgery

If any of the high-risk factors as described above are present or if the MP is not suitable for endoscopic resection, the patient should be counselled for surgery if medically fit. The surgery should involve colectomy with *en bloc* removal of the regional lymph nodes (5). Laparoscopic surgery should be considered if expertise is available as this approach has been shown to be associated with shorter hospital stays and significantly faster recoveries without a difference in long term oncological outcomes (33,34).

## Surveillance

The surveillance strategy would depend on whether the patient underwent surgical resection. For patients who underwent definitive oncological resection of the colon and its draining lymph nodes, the MP should be treated as a stage 1 cancer if none of the lymph nodes were involved and the surveillance strategy should be colonoscopy at 1 year and repeat in 3 years and then every 5 years if there are no advanced adenomas (5). If there are advanced adenomas at the 1-year scope, the colonoscopy should be repeated in 1 year (5). For patients with nodal involvement, they should undergo both cross sectional imaging and endoscopic surveillance along with serial carcinoembryonic antigen testing as per the NCCN guidelines (5).

There is currently no consensus for surveillance of MP treated with endoscopic resection alone. the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society recommends a surveillance scope 3 months post resection and colonoscopy at 1, 3 and 5 years post resection (35). There is a paucity of data on routine imaging surveillance for MP managed with endoscopic resection alone. The group of patients most likely to benefit from routine imaging would be the group with high risk factors for lymph node metastasis but did not undergo oncological resection. The frequency of which should be tailored according to age and co-morbidities of the patient along with the risk of developing nodal metastasis.

## Conclusions

Management of MP is challenging and begins with accurate endoscopic assessment and identifying patients that are suitable for endoscopic resection. Risk of remnant disease and lymph node metastasis should then be evaluated and weighed against the risk of surgery. Patients with high risk features should undergo definitive colectomy with en bloc removal of regional lymph nodes if medically fit. Lastly, timely surveillance should detect recurrences or metachronous lesions early such that curative treatment can be instituted.

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