

CHAPTER 9 MANAGEMENT OF EPITHELIAL POLYPS

A polyp is a circumscribed mass projecting above an epithelial surface. The principal types of epithelial polyp found in the large bowel are:¹

- adenoma or neoplastic polyp
- hyperplastic polyp
- hamartoma (juvenile and Peutz-Jeghers)
- inflammatory.

The term 'polyp' is not synonymous with adenoma. The commonest polyps are the adenoma and the hyperplastic polyp. Although these tend to co-exist within individual patients, only adenomas occur throughout the bowel, whereas hyperplastic polyps are more frequent in the distal colon and rectum. Although distal hyperplastic polyps have been considered to be markers of more proximal adenomas,^{2,3} the larger and better-controlled studies have not found them to be clinically useful in this regard.^{4,5}

Adenomas are usually elevated, and may be sessile or pedunculated. A minority are relatively flat and these may be slightly raised, flat or slightly depressed.^{6,7} Adenomas are typed according to histological architecture as tubular, tubulovillous and villous. They may be diminutive (1–4 mm in diameter), small (5–9 mm) or large (10 mm or more). They are also classified according to the grade of epithelial dysplasia as mild, moderate and severe, or alternatively, as showing low- and high-grade dysplasia.¹ 'Severe' or 'high-grade' dysplasia are terms used in preference to 'carcinoma-in-situ', which has aggressive connotations that are unwarranted.

Evidence for the precancerous nature of the adenoma is well documented in standard texts.⁸

- Adenomas show a spectrum of changes ranging from mild dysplasia through to severe dysplasia.
- Longitudinal studies show malignant progression in (villous) adenomas with time.
- Adenocarcinoma may occur in contiguity with adenoma.
- Epidemiology of adenoma matches adenocarcinoma.
- Genetic changes in adenomas fit with the evolutionary mechanism underlying carcinogenesis.⁹
- Removal of adenomas results in a reduced incidence of adenocarcinoma in non-randomised but controlled studies.¹⁰
- Adenomas in familial adenomatous polyposis (FAP) are identical to sporadic adenomas. FAP patients invariably develop cancer.

9.1 Natural history of adenomas

Based on adenoma prevalence studies from autopsy data and the lifetime cumulative incidence of Colorectal Cancer, it appears that only about 5% of colorectal adenomas undergo malignant transformation.⁸ Adenomas that are more likely to harbour cancer are large and have a villous architecture and/or high grades of dysplasia.⁷ Flat adenomas may possibly be more aggressive or give rise to more aggressive adenocarcinomas.^{11–13}

The clinical context may also influence progression. For example, adenomas occurring in the context of hereditary non-polyposis Colorectal Cancer characteristically show an accelerated evolution.¹⁴ Adenomas may be larger and more numerous in subjects without HNPCC or classical FAP but with a

strong family history of Colorectal Cancer.^{15–17} Serrated polyps showing microsatellite instability may evolve more rapidly to cancer.¹⁸

Most adenomas appear to grow slowly. Small polyps may be observed endoscopically for several years before they are removed and diagnosed histologically.^{19,20} Adenomas under 1 cm, and particularly those measuring 5 mm or less, may remain the same size for years or even regress.^{19,21} The cumulative risk for developing a cancer in polyps (mainly adenomas) greater than 1 cm has been estimated to be 3% at five years, 8% at ten years and 24% at 20 years.²² Studies conducted in different nations have shown that the majority of polyps can be diagnosed from the surface morphology of their pit openings using magnifying endoscopy coupled with indigocarmine dye spraying.^{6,23,24} This approach should yield additional insight into the natural history of adenomas in the future, as well as obviating removal of non-neoplastic polyps.

9.2 Polypectomy

In the absence of magnifying endoscopy combined with dye spraying, it is often not possible to determine the histological type of a polyp by endoscopic inspection.²⁵ Diminutive hyperplastic polyps and adenomas (<5 mm) may be indistinguishable. The unusual large hyperplastic polyp may mimic an adenoma. For this reason, all polyps should be considered for removal. Magnifying endoscopy is likely to become increasingly available and endoscopic diagnosis may reduce the requirement to remove minute polyps in patients with multiple lesions.

Diminutive polyps may be too numerous to be cleared completely. In subjects with multiple small polyps, a sample of at least three should be biopsied for histological study.^{26,27} Hot biopsy and electrocoagulation have been used to eradicate diminutive polyps, but may leave residual polyp tissue behind.^{28–31} Cold snare polypectomy is an effective alternative,³² it does not compromise histology but compromises recovery of tissue for histopathology. Cancer risk is related to number of adenomas, so the documentation of polyp type has prognostic value and surveillance implications.

Polyps should be removed. Sessile polyps may require piecemeal removal, but this will make histological evaluation difficult or impossible.³³ The area may be tattooed with sterile India ink to facilitate follow-up evaluation.³⁴ Tattooing will also identify the site for subsequent surgical resection.

9.3 Malignant polyps

This term applies to an adenoma containing a focus of malignancy. Management of malignant polyps by polypectomy alone is now standard practice and is generally acknowledged to be safe, providing a strict policy of case selection and histopathological assessment is adhered to.^{35–38} For example, polyps containing poorly differentiated adenocarcinoma are not suitable for curative local excision in view of the high risk of associated lymph node metastasis.³⁹

Attempts to identify factors indicative of lymph node spread, local recurrence and prognosis in patients treated by endoscopic (colonoscopic) polypectomy for a malignant polyp and then managed by either follow up alone or surgical resection have identified four key factors that are linked to a favourable outcome:

- a clear margin of excision
- well or moderate cancer differentiation
- absence of lymphatic or venous invasion
- endoscopic assessment of total removal.

Although the usefulness of lymphatic invasion³⁷ and venous invasion^{36,37,40} has been questioned, and is a rare finding in the absence of other unfavourable features, it is advisable that vessel invasion continue to be regarded as an adverse marker.^{36,41–43}

While polyp size, extent of replacement by cancer and a sessile base are factors that may impede complete local excision and definitive histopathological assessment, it is the fact of demonstrable complete or incomplete excision that serves as an independent predictor of outcome.^{36,37} The pathologist is required to examine multiple-step sections through the polyp base to make this determination. If this is done with care, the majority of cases can be classified as either completely or incompletely excised. A specific clearance margin of 1 mm³⁶ or 2 mm³⁷ has been advocated, but the importance of achieving such margins has not been evaluated. In one study, nine subjects had a clear margin, but cancer was within 2 mm of the line of excision. Only one of these patients turned out to have residual cancer, but it was not stated whether this was within the polyp base or a lymph node.³⁷ Pathologists are generally comfortable with reporting a surgical margin as either clear or not clear.

Malignant polyps with unfavourable features may require further treatment, but this decision should be made on the basis of the age, health and wishes of the patient. Treatment decisions will also be influenced by site, particularly in the case of low rectal lesions for which radical surgery would involve abdominoperineal excision and colostomy. For colonic polyps, excision can be achieved successfully by laparotomy with colonic resection or laparoscopically assisted colectomy.⁴⁴ (See also Chapter 11.)

9.4 Follow-up surveillance for adenomas

Patients developing adenoma or carcinoma are at increased risk of developing additional (metachronous) neoplasms in the future.

9.4.1 Adenoma follow up

There are no internationally agreed recommendations for following up patients with adenomas.

Close endoscopic follow up should follow piecemeal removal or excision of a large adenoma or a malignant polyp that may have been incompletely removed.

In a British study, 1618 patients were treated for rectosigmoid adenomas using rigid-instrument sigmoidoscopy. The long-term risk of developing Colorectal Cancer was assessed in retrospect. The incidence of rectal cancer was similar to that of the general population. Most rectal cancers occurred in subjects with incompletely excised adenomas. The risk of colon cancer depended on the type, size and numbers of rectosigmoid adenomas removed initially. An increased standardised incidence ratio of 3.6 was observed in subjects with large adenomas (>1 cm) or adenomas with a villous component. The ratio was increased to 6.6 if, in addition, subjects had multiple adenomas. In the remaining subjects with small excised tubular adenomas, the risk of cancer was not increased, even in subjects with multiple adenomas (standardised incidence ratio = 0.5).⁴⁵ This study suggests that a sizeable subset of patients with small (<1 cm) tubular adenomas that have been removed from the rectosigmoid region is not at increased risk of developing significant colorectal neoplasia in the future. However, it was not a prospective study and relates only to patients with excised adenomas of the distal large bowel.

The United States National Polyp Study has confirmed that risk factors for metachronous colorectal neoplasia include adenoma size, presence of villous change and multiplicity.⁴⁶ This study also advocates an interval of at least three years before re-endoscopy, as adenoma recurrence rates were no higher when intervals of three years were compared to one year. A longer follow-up interval of six years has been proposed for subjects *other* than those:

with three or more adenomas at initial colonoscopy, or

- who are 60 or over and have a parent with Colorectal Cancer.

A screening interval of 4–6 years is recommended for this low-risk group and three years for the two high-risk groups. High-risk subjects should also include those with ≥ 1 cm adenomas and adenomas with high-grade dysplasia or villous change. The relative risk of developing a significant adenoma (>1 cm) or having high-grade dysplasia or invasive cancer was 5.2 and 4.3 for the high-risk groups respectively. The two high-risk groups accounted for 69% of significant adenomas and 27% of the subjects in the study.⁴⁷

In summary, a three-yearly follow-up period is safe, provided colonoscopy is complete, the endoscopist has removed all polyps seen and is confident of adequate visualisation. It may be extended further for subjects lacking high-risk features.^{26–28,45–48}

What is the management of epithelial polyps?

Guidelines — Management of epithelial polyps	Level of evidence	Practice recommendation	Refs
All polyps should be at least sampled, and preferably removed. Synchronous polyps should be sought and removed.	III-2	Recommend	25–34

What is the general management of all patients with colorectal neoplasia completely removed at colonoscopy?

Guidelines — Management of epithelial polyps	Level of evidence	Practice recommendation	Refs
All patients with colorectal neoplasia completely removed at colonoscopy should then be considered for colonoscopic surveillance according to the following protocols:			
<ul style="list-style-type: none"> • within a year following incomplete or possible inadequate examination, for example in a subject with multiple adenomas 	II	Recommend	45–48
<ul style="list-style-type: none"> • at three years for subjects with large adenomas (>1 cm), adenomas with high-grade dysplasia, villous change in adenomas, three or more adenomas, or aged 60 or more with a first-degree relative with colorectal neoplasia 	II	Recommend	
<ul style="list-style-type: none"> • at four to six years in subjects without the risk factors outlined above. 	III-3	Equivocal	

What is the management of malignant adenomas?

Guidelines — Management of malignant polyps	Level of evidence	Practice recommendation	Refs
Malignant adenomas may be managed safely by endoscopic polypectomy provided strict criteria for patient selection and histopathological assessment are adhered to. In particular, malignant adenomas should be well or moderately differentiated and excision should be complete.	III-2	Recommend	35–43

9.4.2 Other polyposis conditions

A situation in which the hyperplastic polyp may be a marker for cancer risk is one involving subjects with hyperplastic polyposis.⁴⁹ In this condition, hyperplastic polyps are large, often exceeding the usual limit of 5 mm, and occur throughout the bowel. It has been suggested that the polyps occurring in hyperplastic polyposis are actually serrated adenomas. The term ‘serrated adenomatous polyposis’ is probably synonymous with hyperplastic polyposis.⁵⁰ There is evidence linking hyperplastic polyps, mixed polyps and serrated adenoma (serrated polyps) with a subset of sporadic Colorectal Cancer showing high-level DNA microsatellite instability (MSI-H).^{51–54} Sporadic MSI-H cancers are age-related, occur more frequently in females, are mainly located in the proximal colon, and account for about 10% of Colorectal Cancer and some are associated with multiple hyperplastic and/or serrated adenomatous polyps.⁵⁵

Although solitary juvenile polyps are not precancerous, juvenile polyposis, a rare condition that may occur as an autosomal dominant trait, is associated with an increased risk of malignancy.⁵⁶ Malignancy in the Peutz-Jeghers syndrome is usually extracolonic, but there is a small increased risk of Colorectal Cancer.⁵³

9.5 Hyperplastic polyps and polyposis

Hyperplastic polyps are usually small, innocuous lesions limited to the distal colon and rectum. However, there are 11 reports of Colorectal Cancer arising in sporadic hyperplastic polyps. These polyps have been large and mainly right-sided.⁵⁷ It is likely that most of these large hyperplastic polyps are identical to the recently documented entity described as ‘sessile serrated adenoma’.^{58–60} These variant hyperplastic polyps are over-represented in the condition hyperplastic polyposis.⁵⁰ Patients with multiple hyperplastic polyps and/or large hyperplastic polyps and/or hyperplastic polyps of the proximal colon are at increased risk of cancer.^{50,61–63} The risk may be further increased if there are co-existing adenomatous lesions that may be traditional adenomas, admixed polyps or serrated adenomas, or if there is a family history of Colorectal Cancer.^{64,65} A particular association has been demonstrated between hyperplastic polyps and cancers with microsatellite instability.^{51,52,54,66,67} The term ‘hyperplastic polyposis’ has been applied to two phenotypes: (i) presence of at least 20–30 hyperplastic polyps proximal to the rectosigmoid junction, (ii) at least five hyperplastic polyps proximal to the splenic flexure, of which two are larger than 1 cm.^{68,69} However, patients with other combinations of features may also be at increased risk.⁷⁰

Genetic studies are beginning to delineate heterogeneity among hyperplastic polyps.^{18,69} DNA methylation, leading to gene silencing, is more frequent when there are large hyperplastic polyps, hyperplastic polyps of the proximal colon and co-existing serrated adenomas.^{71,72} When one polyp is found to show DNA methylation, the same usually applies to all (implying a generalised or field defect).⁷¹ K-ras mutation or loss of chromosome 1p is more common in sporadic hyperplastic polyps and in patients with hyperplastic polyposis in which polyps are left-sided, small and there are no associated serrated adenomas.^{69,71} Large, right-sided hyperplastic polyps are more likely to have

BRAF mutation, particularly when multiple or having the morphological features of sessile serrated adenoma.⁷³ BRAF mutation also occurs in traditional serrated adenomas.⁷⁴

It is recommended that patients with hyperplastic polyposis be offered annual colonoscopy. This should also be considered for patients in whom neither of the strict definitions for the diagnosis of hyperplastic polyposis is met in full, but other risk features are present (one coexisting adenomatous lesion or a first-degree relative with hyperplastic polyposis or Colorectal Cancer). Colectomy should be considered when it is not possible to achieve control of polyps endoscopically. There is increasing evidence that sporadic hyperplastic polyps have malignant potential, particularly when they are large, proximally located, and have the morphological appearances associated with sessile serrated adenoma.^{58-60,75,76}

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