COLORECTAL CANCER SCREENING

Surveillance guidelines after removal of colorectal adenomatous polyps

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Most colon cancers are assumed to have a premalignant adenomatous polyp phase, therefore colonoscopic detection and polypectomy provides the opportunity for cancer prevention. Some patients who have undergone colonoscopy and have had adenomas removed are at increased risk of developing colorectal cancer (CRC) in the future, and therefore might benefit from colonoscopic surveillance. However, it is important to appreciate that colonoscopy is an invasive and costly procedure with some associated morbidity. It is also an under-resourced procedure in the UK, with a serious lack of fully trained endoscopists. Around one third of the population will develop an adenoma by age 60. Most adenomas are asymptomatic and remain undiagnosed. If colorectal screening is introduced this situation will change dramatically. There are few data on the benefits of colonoscopic surveillance in preventing colorectal cancer after a baseline clearing colonoscopy. It is therefore important that this practice is applied judiciously, balancing the risks and benefits in each individual case. Using published evidence, this guideline recommends appropriate surveillance after adenoma removal. The decision to perform each follow up colonoscopy should also depend on the patient’s wishes, the presence of comorbidity, the patient’s age, and the presence of other risk factors.

EXECUTIVE SUMMARY

Risk of colorectal cancer and adenomas with advanced pathology (≥1 cm or severely dysplastic) (see fig 1)

Risk can be stratified according to findings at baseline and refined at each subsequent surveillance examination.

(Recommendation Grade B)

Low risk

Patients with only 1–2, small (<1 cm) adenomas.

Recommendation: no follow up or five yearly until one negative examination.

Intermediate risk

Patients with 3–4 small adenomas or at least one ≥1 cm

Recommendation: three yearly until two consecutive negative examinations.

High risk

If either of the following are detected at any single examination (at baseline or follow up):

≥5 adenomas or ≥3 adenomas at least one of which is ≥1 cm.

Recommendation: An extra examination should be undertaken at 12 months before returning to three yearly surveillance

Stopping surveillance due to comorbidity or age

The cut off age for stopping surveillance is usually 75 years, but should also depend upon patient wishes and comorbidity.

(Recommendation Grade C)

Incomplete examinations

Patients with failed colonoscopies, for whatever reason, should undergo repeat colonoscopy or an alternative complete colon examination. These guidelines are based on accurate detection of adenomas; otherwise risk status will be underestimated.

Large sessile lesions

Large sessile adenomas removed piecemeal should be re-examined at three months. Small areas of residual polyp can be retreated endoscopically, with a further check for complete eradication in three months. If extensive residual polyp is seen, open surgical resection needs to be considered. If there is complete healing of the polypectomy site, then there should be a sigmoidoscopy or colonoscopy at one year before returning to three yearly surveillance. India ink tattooing aids recognition of the polypectomy site at follow up.

THE NATURAL HISTORY OF COLONIC POLYPS

The concept that most cancers arise from pre-existing adenomas is now widely accepted, based on epidemiological, clinical, postmortem, and molecular biological studies. Synchronous adenomas and cancers are a common finding as adenomas with a focus of malignancy. Adenomas are diagnosed on average 10 years earlier than CRCs, providing temporal evidence for the adenoma-carcinoma sequence. Genetic changes have been identified that seem to promote the growth of adenomas and their malignant transformation. Postmortem and screening colonoscopy studies estimate the prevalence of colonic adenomas to be 30%–40% at age 60 years, however the lifetime cumulative incidence of CRC is 5.5% therefore many colonic adenomas do not progress to cancer. Small adenomas are rarely malignant, however the malignant potential increases with increasing size. The development of invasive cancer from a small (<10 mm) adenoma is unlikely in less than five years. A barium enema study, before the colonoscopy era, of large polyps (≥1 cm), left in situ, has shown the cumulative risk of malignancy at 5, 10, and 20 years to be 2.5%, 8%, and 24%. The exception to this slow progression may be flat or depressed adenomas, which may progress more rapidly than polyoid adenomas to cancer. Small flat cancers have been reported to account for 10%–30% of CRC in Japan, but are still an uncommon finding in the West. Flat adenomas and cancers are easy to miss during conventional endoscopy and the true incidence in the West has yet to be determined.

EVIDENCE THAT COLONOSCOPIC POLYPECTOMY PREVENTS CANCER

Although there is no direct evidence that endoscopic polypectomy reduces cancer mortality, there is a wealth of observational evidence demonstrating a likely benefit. The USA National Polyp Study observed a 70%–90% lower than expected incidence of CRC in patients undergoing colonoscopic surveillance compared with three reference populations. Several studies have shown reductions in incidence and mortality rates of distal colorectal cancer after sigmoidoscopy screening of the order of 60–80%. A single screening endoscopy seems to confer protection of 6–10 years.
There have been no randomised trials examining the benefit of colonoscopy surveillance after adenoma detection. Independent studies undertaken on the US National Polyp Study dataset showed that the observed reduction in incidence of colorectal cancer could be accounted for entirely by the initial colonoscopic polypectomy. Thus this study does not provide evidence that colonoscopic surveillance reduces risk further than achieved by the initial clearing colonoscopy.

**COLONOSCOPY AND POLYPECTOMY**

Colonoscopy provides detailed views of most of the colonic surface and is currently the gold standard examination for the detection and removal of colonic polyps. It has greater sensitivity than barium enema for both polyps and cancer and permits simultaneous excision of polyps, thereby having the advantage of being both diagnostic and therapeutic. Passage of the colonoscope to the caecum, careful inspection of the mucosal surface during withdrawal, and safe removal of colonic polyps are the main aims of colonoscopy. Colonoscopy with or without polypectomy is, however, an invasive procedure requiring bowel preparation, considerable cooperation from the patient, and has a small risk of major complication, either from perforation (0.06% to 2.0% overall) or major haemorrhage after polypectomy (0.4%–2.7%).

**EVIDENCE TO SUPPORT THE GUIDELINES**

**Rationale for colonoscopic surveillance after adenoma detection**

Patients who have adenomas completely excised from the rectum and distal sigmoid colon via the rigid sigmoidoscope have on average a twofold increased risk of developing colon cancer, but have no increased risk of developing rectal cancer. The residual risk of colorectal cancer after removal of adenomas at colonoscopy is not known. It is possible that most patients are at very low risk after an initial colonoscopy with polypectomy of all detected lesions.

The rationale for colonoscopic surveillance has always been based on the high detection rate of colorectal adenomas at follow up (30%–50%) after a complete clearance colonoscopy. However, the main object of colonoscopic surveillance is the prevention of subsequent colorectal cancer rather than the detection and removal of adenomas, most of which will not become malignant. Adenomas with advanced pathology (2 cm, with villous elements or severe dysplasia) have a much higher malignant potential and the object of screening is to ensure that such lesions are detected before they become invasive.

The US National Polyp Study was a randomised comparison of different surveillance intervals in 1418 patients with newly diagnosed adenomas removed at colonoscopy. In this study the observed reduction in incidence of colorectal cancer could be accounted for entirely by the initial colonoscopic polypectomy.
The longer term risk of developing colorectal cancer also seems to be low for such patients. No increased incidence of cancer was observed in 751 patients after removal of small (1 cm or less) colorectal polyps; 17% of which were unexamined histologically. A similar study from St Mark’s Hospital, in which all removed polyps were examined histologically, found that patients from whom only small (<1 cm) tubular adenomas were removed had no increased risk of developing colon cancer long term. Risk of rectal cancer was profoundly decreased compared with the unexamined population. Thus it seems that whether the outcome is an advanced adenoma or cancer, future risk is low among patients with one to two small adenomas. There is uncertainty as to the role of histology as a predictor of future risk. Histological subtyping of adenomas is subjective and the reproducibility is poor. The WHO criteria34 for the presence of tubulovillous or villous histology stipulates the finding of villous elements in more than 20% of the specimen. Sampling errors in small biopsies exacerbate difficulties in interpretation.

Available results suggest that the benefits compared with the risks of surveillance colonoscopy are likely to be small in patients with only one to two small adenomas, and that follow up colonoscopy, if undertaken at all, should be delayed at least five years.

The reason we suggest surveillance at all for this group is that there is no routine screening programme to otherwise assess them in follow up. If a screening programme is introduced, it will identify many people with one to two small adenomas, and it will not be feasible or appropriate to routinely offer them surveillance as they can be managed adequately by continued population screening.

Significance of a normal surveillance colonoscopy
Khoury35 undertook a retrospective examination of 389 patients who had undergone follow up colonoscopy at one year intervals after resection of colorectal cancer. The adenoma detection rate at follow up was 10% at one year if the prior colonoscopy was negative and 40% if the prior colonoscopy was positive. If multiple adenomas were found at the prior examination, 70% of colonoscopies were positive. Similarly in patients with a history of adenomas, a normal follow up colonoscopy was associated with a lower incidence of subsequent adenomas at the next colonoscopy. Risk of advanced adenomas was reported by the National Polyp Study36 to be higher after detection of adenomas at the first follow up, although no data were published.

None of the studies to date has provided evidence to inform guidelines on the degree of protection afforded by a single negative follow up examination in patients with “high risk” adenomas at baseline. One study17 has shown that a negative result at first follow up examination in patients with multiple adenomas initially does not preclude the subsequent development of new adenomas. Thus, until data to the contrary are available, it must be assumed that patients with “high risk” adenomas remain at increased risk despite a single negative follow up examination. After two consecutive negative examinations there can be greater confidence that adenomas have not been missed and that subsequent risk is decreased.
This suggests that surveillance can cease following a single negative follow up colonoscopy in lower risk patients, but that two negative examinations are required for higher risk patients.

STOPPING SURVEILLANCE
The cut off age for stopping surveillance is usually quoted as 75 years as the remaining life expectancy is likely to be less than the average time required for new adenomas to become malignant. After this age, it is unlikely that the benefits of surveillance will outweigh the potential risks of the procedure. However, this should not preclude further surveillance in a fit and motivated person who has a tendency to produce multiple or advanced adenomas at follow up.

The risks and benefits of adenoma surveillance need to be balanced at all ages, particularly in patients who have significant comorbidity. The patient status should be established prior to surveillance guidelines after removal of colorectal adenomatous polyps v9...