

# Screening and surveillance for upper and lower gastrointestinal cancer

JN Plevris

Consultant Gastroenterologist and Honorary Senior Lecturer, Centre for Liver and Digestive Disorders, Royal Infirmary, Edinburgh, Scotland

**ABSTRACT** Cancers of the GI tract are the most common cancers in Europe and the US. Surveillance is recommended in Barrett's oesophagus, gastric atrophy, and inflammatory bowel disease. For Barrett's oesophagus, 3–5-yearly endoscopic surveillance is appropriate. The natural history of colorectal cancer justifies screening the general population or certain high-risk groups. The most widely accepted screening method is FOBT followed by colonoscopy if the FOBT is positive. In patients with excised adenomatous polyps, repeat colonoscopy is recommended in 3 years if high risk and 5 years if low risk. Surveillance is justifiable up to 75 years of age if there is no significant co-morbidity. Colonoscopic surveillance in inflammatory bowel disease starts 10 years from diagnosis for pancolitis and 15 years from diagnosis for left-sided colitis; thereafter every 3 years. Asymptomatic patients with strong family history of colorectal cancer should be referred to a clinical geneticist for risk assessment prior to colonoscopy screening.

**KEYWORDS** Adenomatous polyps, Barrett's oesophagus, colorectal cancer, gastric cancer, inflammatory bowel disease, oesophageal cancer

**LIST OF ABBREVIATIONS** adenomatous polyposis coli (APC), faecal occult blood testing (FOBT), familial adenomatous polyposis (FAP), gastrointestinal (GI), hereditary non-polyposis colonic cancer (HNPCC)

**DECLARATION OF INTERESTS** No conflict of interests declared.

## OVERVIEW

### Introduction

Cancers of the GI tract are the most common cancers in Europe and the US. Over half arise from the colon, with oesophagogastric and pancreatic cancers the next most common. Overall, colorectal is one of the most common cancers, exceeding lung or breast cancers in Europe, and falling behind lung, breast, and prostate cancers in the US. In the Western world, 25% of mortality is attributable to cancer, and half of this is due to colorectal cancer.

The last three decades have seen significant changes in the demographics of upper GI cancer. The incidence of oesophageal squamous cell carcinoma (usually affecting the middle third) and distal gastric carcinoma has been declining, while adenocarcinoma of the oesophagus (usually affecting the lower third) and proximal stomach has been rising, particularly in males. Obesity and chronic gastro-oesophageal reflux have been implicated in this rise. Metaplasia to specialised intestinal epithelium secondary to a maladaptive response to acid-related mucosal injury in the lower part of the oesophagus (Barrett's oesophagus) is a recognised risk factor.

The incidence of colorectal cancer remains high in the Western world. Both genetic susceptibility and environmental factors are important in the development of the condition, although approximately two-thirds of the incidence is due to a diet high in animal fat and red meat combined with low fibre (fruit and vegetables) intake.

Unfortunately, both upper and lower GI cancer remain relatively asymptomatic until late in the natural history of the disease. Upper GI cancer symptoms are often non-specific and by the time that 'alarm symptoms' such as dysphagia, abdominal pain, vomiting, weight loss, or anaemia are present, cancer is often at an advanced stage and the prognosis is poor. In particular, colorectal cancer can be completely asymptomatic during the stage of malignant transformation of pre-existing adenomatous polyps to cancer, and it is at that point of the disease that the cancer can be cured.

The natural history of colorectal cancer justifies screening the general population or at least certain high-risk groups, aiming at early diagnosis when complete cure is possible. It is also increasingly accepted that pre-malignant conditions, such as Barrett's oesophagus, gastric atrophy, inflammatory bowel disease, or adenomatous colonic polyps, justify surveillance for progression to cancer.

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Correspondence to JN Plevris, Centre for Liver & Digestive Disorders, The Royal Infirmary of Edinburgh, Little France Crescent, Edinburgh EH16 4SA

tel. +44 (0)131 242 1631

e-mail J.Plevris@ed.ac.uk

## Screening and surveillance for oesophagogastric malignancy

### Gastric cancer

Screening for early gastric cancer is common in Japan due to the high incidence of the disease in that country. In Europe and the US, the overall decline of gastric cancer and the high costs of screening the general population do not favour such screening. Endoscopic screening and subsequent surveillance, however, is recommended by some for patients with a family history of gastric cancer or HNPCC, pernicious anaemia, gastric atrophy, and long-standing partial gastrectomy.

### Barrett's oesophagus

Screening otherwise well individuals for Barrett's oesophagus is not widely recommended because of lack of unequivocal evidence that screening has any significant impact on life expectancy. Barrett's oesophagus is a relatively common condition, affecting 1–5 % of the population, and in most cases it remains undetected during life. Although it is considered a pre-malignant condition (40-fold risk increase), the estimated incidence of adenocarcinoma in Barrett's oesophagus is small and varies from one cancer per 48 patient-years to one per 440 patient-years of surveillance.

There is no general agreement on the value of endoscopic surveillance of Barrett's oesophagus and it has not been universally endorsed, partly due to cost but also because of uncertainty about the pick-up rate for cancers and the fact that this is a predominantly elderly population. The estimated cost of detecting cancer that arises from Barrett's oesophagus in the UK varies from £15,000–£42,000. Despite initial reservations, however, surveillance has become more accepted in the last 5 years because of evidence from US studies that there is a small potential gain in life expectancy for surveyed patients. Further studies taking into account cost, risks, and impact on length and quality of life recommend 3–5-yearly endoscopic surveillance as the most viable strategy, provided that there is no dysplasia on biopsy. Surveillance is justifiable up to 75 years if there is no significant co-morbidity.

Where dysplasia has been detected, more intensive surveillance is recommended. Mild dysplasia is often due to inflammation secondary to acid reflux and usually resolves after treatment with proton pump inhibitors. Endoscopy should be repeated when dysplasia is still present after 6 months of treatment and yearly thereafter if it is still present. Severe (high-grade) dysplasia, if persistent and confirmed by two independent pathologists, carries a high risk of progression to cancer and intensive surveillance (3 monthly) is recommended. Persistence of severe dysplasia is best managed by oesophagectomy because of the high probability of co-existing cancer (50% approximately).

Patients with Barrett's oesophagus should be advised to stop smoking and reduce alcohol consumption.

### Screening for colorectal cancer

The high incidence of colorectal cancer justifies screening of people over 50 and up to 75 years of age, provided there is no significant co-morbidity to preclude surgery. Screening is being applied to general populations and to high-risk groups such as patients with a strong family history of colorectal cancer and therefore genetic predisposition, and patients with inflammatory bowel disease or acromegaly. Surveillance by colonoscopy is necessary for those in high-risk groups as well as for those from the general population with diagnosed adenomatous polyps or for patients previously treated for colorectal cancer.

### Population screening

The most widely accepted screening method is FOBT followed by colonoscopy if the FOBT is positive. FOBT screening has been shown to reduce colorectal cancer mortality by 16%, and when adjusted for failure to attend screening, by 23%. Despite a lack of evidence for superiority in cost-effectiveness over other screening options, colonoscopy is the preferred screening method in the US. A suggested plan includes a single colonoscopy over the age of 50 years and at 10-yearly intervals thereafter. Implementation of such protocols, however, is difficult due to the significant resources required, particularly notable in the UK in the context of a national health service. Alternatives include FOBT with flexible sigmoidoscopy or once-only flexible sigmoidoscopy. Clinical algorithms have also been suggested to focus attention on individuals at increased risk, for whom colonoscopic surveillance may be best. At present, FOBT screening appears to be the most cost-effective and realistic approach. Over the next 3 years the results of several trials around the world hopefully will provide important information to facilitate selection of the optimum screening method.

### Patients with inflammatory bowel disease

Patients with long-standing ulcerative colitis are at higher risk of developing colorectal cancer than the general population (see also Recognition and management of inflammatory bowel disease by S Ghosh). The overall incidence of cancer in patients with inflammatory bowel disease is approximately 4%, but there is an exponential increase in the cumulative probability of cancer development with time, ranging from 2% at 10 years to 18% at 30 years. Crohn's colitis carries similar risks to ulcerative colitis. Colonoscopic surveillance is usually initiated at 10 years from diagnosis for pancolitis and at 15 years from diagnosis for left-sided colitis and thereafter at 3-yearly intervals. After 20 years of disease or if dysplasia

is present at any point, yearly surveillance is recommended. It is extremely important that several biopsies are taken along the bowel in addition to biopsies from suspicious lesions to look for dysplastic changes. Total colectomy is the treatment of choice for high-grade dysplasia, and should also be considered for low-grade dysplasia. This decision is often difficult and requires a consensus between the patient and the caring physician.

#### *Patients with family history of colorectal cancer*

There are no clear recommendations for screening asymptomatic individuals on the basis of a family history of colorectal cancer. As a guide, a patient with positive family history at the age of 40 has the same cancer risk as someone without a family history who is 50 years old. In particular, someone who is over the age of 45 with one first-degree relative or with one or more second-degree relatives affected with cancer is not at any higher risk than a member of the general population to develop colorectal cancer.

#### *Patients with HNPCC*

Patients from families with HNPCC, with two or more affected first-degree relatives or one first-degree relative under 45 years of age affected, are at higher cancer risk and should be referred for genetic counselling and risk assessment by a clinical geneticist. It is very important that the referring physician takes a three-generation family history for colorectal cancer. Patients are often not aware of HNPCC in their family, but the following can be used as a guide: at least three individuals affected by colon cancer or two affected by colon cancer and another by uterine cancer; there should also be evidence of involvement in two or more generations; one relative should be a first-degree relative of the other two; and at least one affected relative should be less than 50 years old. Patient age is also important in risk calculation; any patient with a high-risk family history as defined above has a particularly high risk if he or she is less than 45 years old. Following risk stratification, the currently recommended screening strategy is presented in Table 1.

#### *Patients with familial adenomatous polyposis*

Familial adenomatous polyposis is an autosomal dominant condition due to an APC gene mutation. Multiple adenomatous colorectal polyps are frequently present from an early age with subsequent development of colorectal cancer, often before the age of 30. Patients with a clinical diagnosis of FAP should be referred to clinical genetics for APC mutation studies. Patients at risk of FAP should have surveillance colonoscopy indefinitely every 3 years and yearly sigmoidoscopy. Surgery (total colectomy) should be offered to these patients once adenomas have developed.

#### *Surveillance of patients with adenomatous polyps*

Most colorectal cancers arise from adenomatous polyps. Metaplastic polyps do not have any malignant potential. Simple (i.e. without villous component) and small (<1 cm) tubular adenomas are very common and have a low malignant potential. Advanced adenomas carry the highest risk of malignant transformation and are defined as being >1 cm, containing villous tissue, and with evidence of high-grade dysplasia.

#### *Small polyps*

Small polyps (<1 cm) are usually easily resectable endoscopically. When small polyps are numerous, representative biopsies should be taken and full colonoscopy is advisable if they were detected during flexible sigmoidoscopy. Controversy exists as to whether small distal adenomas predict the presence of proximal, clinically significant adenomas; colonoscopy is generally advisable if >1 small adenomatous polyp is seen at flexible sigmoidoscopy.

#### *Large polyps*

Following successful colonoscopic excision of a large adenomatous polyp (>1 cm), a follow-up colonoscopy in 3–6 months is advisable to determine whether resection has been complete, unless there is unequivocal evidence from pathology that the polyp has been completely excised. This is particularly important for polyps with broad bases. If a residual polyp is present, it should be resected and the completeness of resection should be rechecked in another 3–6 months. If complete resection is not possible after two examinations, the patient should be referred for surgery.

#### *Surveillance*

After the complete removal of polyps at an initial colonoscopy, a repeat colonoscopy to check for new adenomas is recommended in 3 years for patients at high risk. These are patients who at initial examination have multiple adenomas (>2), large adenoma (>1 cm), or an adenoma with a villous component at histology or high-grade dysplasia. If colonoscopy is normal on two consecutive occasions no further surveillance is necessary thereafter.

Repeat colonoscopy to check for other adenomas should be performed in 5 years for patients at low risk. These are patients who at baseline examination have only 1 or 2 small tubular adenomas (<1 cm) and no family history of colorectal cancer. After one negative follow-up colonoscopy at 5 years, surveillance can cease.

Surveillance should be individualised according to the age (in general, surveillance may not be appropriate for patients over 75 years) and co-morbidity of the patient, and should be discontinued when it seems unlikely that follow-up would either prolong or improve quality of life.

### Surveillance of malignant polyps

No further immediate treatment is indicated after colonoscopic resection of a malignant polyp if the polyp has been completely excised (as shown by histological examination), the cancer is not poorly differentiated, and there is no vascular or lymphatic involvement. If there is uncertainty a repeat examination at 3–6 months is necessary, and if that is negative, standard surveillance as per adenomatous polyps should be applied. If the polyp is not completely excised after the second colonoscopy, surgery should be considered.

### Surveillance following resection for colorectal cancer

Prior to resection, the yield for synchronous colorectal cancer is approximately 2% and for adenomas 25%. Provided that all synchronous lesions are removed prior to surgery, surveillance should be performed at 1 year from date of surgery, thereafter at 3 years and, if clear, at 5-yearly intervals.

**TABLE 1** Guidelines on frequency of screening colonoscopy in asymptomatic patients with a strong family history of colorectal cancer (CRC) (adapted from SIGN Guideline No 67, courtesy of Professor M. Dunlop, Colon Cancer Genetics Group, University of Edinburgh)

Risk level	Criteria for referral and screening*	Screening	Age to begin	Age to end
Low risk	Anyone not fulfilling medium or high-risk criteria	Reassure/healthy lifestyle Return to GP's care		
Medium risk	One first-degree relative affected by colorectal cancer when aged < 45 years;  Two (one CRC less than 55 years) or three affected with colorectal or endometrial cancer who are first-degree relatives of each other and one a first-degree relative of consultee;  Two affected first degree relatives (1 less than 55 years)	Single colonoscopy if normal findings  Single repeat colonoscopy (incomplete colonoscopy should be followed by a barium enema)	30–35 years and again at 55 years	
High risk	Greater than three family members affected by CRC or greater than two with CRC and one with endometrial cancer in greater than two generations; one affected relative must be age less than 50 at diagnosis; one of the relatives must be a first-degree relative of the other two.  Gene carriers (HNPCC genes)  Untested first degree relatives of gene carriers	Colonoscopy every 2 years  Discuss gynaecological screening for endometrial and ovarian cancer  Offer 2-yearly GI endoscopy for gastric cancer  Consideration needs to be given to other screening for other cancers which may occur in specific families and are part of the HNPCC spectrum.  Discuss prophylactic surgery for bowel and hysterectomy with bilateral oophorectomy.  For established colorectal and associated cancer discuss extent of surgery	From 30 years or 5 years younger than the youngest affected  For stomach cancer from 50 years or 5 years younger than the youngest affected with stomach cancer	70

\* Multiple polyps (3 or more adenomas) in an individual with one of the above criteria for medium and high-risk may be regarded as 'affected'

## HIGHLIGHTS

- Cancer of the GI tract is the most common cancer in Europe. Over half of GI cancer cases arise from the colon.
- The incidence of oesophageal squamous cell carcinoma and distal gastric carcinoma has been declining, while adenocarcinoma of the oesophagus and proximal stomach has been rising.
- The most widely accepted population screening modality for colorectal cancer is FOBT followed by colonoscopy if FOBT is positive.
- For Barrett's oesophagus 3–5-yearly endoscopic surveillance is recommended, or more frequently if there is evidence of dysplasia on biopsy.
- Colonoscopic surveillance in inflammatory bowel disease at 3-yearly intervals, starting at 10 years for pancolitis and at 15 years for left-sided colitis is recommended. Surveillance frequency is increased to yearly after 20 years of disease.
- Asymptomatic patients with a strong family history of colorectal cancer should be referred for risk assessment by a clinical geneticist. Colonoscopy screening and subsequent surveillance at appropriate intervals depending on risk is necessary.
- In patients with excised adenomatous polyps, surveillance colonoscopy is recommended in 3 years for high-risk, and at 5 years for low-risk, patients.

## FURTHER READING

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