Bowel cancer screening

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Abstract

Colorectal cancer (CRC) is the third most common cancer in both males and females in the UK giving rise to approximately 40,000 new cancer cases per year. It arises from polyps as part of the adenoma-carcinoma sequence. Early detection can aid treatment and improve outcomes. Faecal occult blood (FOBt) and direct imaging using colonoscopy/sigmoidoscopy has been shown to be advantageous in the detection of polyps and earlier cancer. We review the evidence and provide summaries of current strategies as well as future potential developments.

Keywords Colorectal cancer; polyps; screening

Why is a bowel cancer-screening programme important?

Colorectal cancer (CRC) is the third most common cancer in both males and females in the UK giving rise to approximately 40,000 new cancer cases per year.[1] About 21% of colorectal cancers present as emergency admissions.[2] Outcomes for these patients when compared to those managed electively are poorer. They generally present with more advanced disease: only 9.8% of emergency cancers have early disease compared to 34.6% in the screened group.[2] About 52% of those with an emergency presentation are treated with curative intent compared to 90% of cases in the screened group.[2] Surgical 90-day mortality is starkly different with a rate of 13% in the emergency group versus 3.8% in the elective group.[2] These facts alone provide a compelling argument for early intervention and therefore a national bowel cancer-screening programme.

CRC – an important health problem

As previously outlined, CRC is an 'important health problem' accounting for approximately 40,000 new cancer cases and 16,000 deaths each year.[1] Six out of ten cancers are diagnosed in patients aged 70 or over.[1] Symptoms suggestive of a CRC include rectal bleeding, change in bowel habit, tenesmus, anaemia and weight loss.

Natural history of CRC

Most CRC are adenocarcinomas and are thought to arise from normal colonic mucosa through a series of cumulative mutations causing their transformation into an adenoma. This initial phase is associated with the loss of the tumour suppressor gene, adenomatous polyposis coli (APC) gene.[3] As the adenoma progresses through its early to late phase it accumulates more mutations causing chromosomal instability[3] perpetuating and furthering dysplastic changes until a frank carcinoma develops. This is known as the adenoma-carcinoma sequence (Figure 1).

Does early intervention change outcome?

The phase between an early and a late adenoma is estimated to be 5–10 years.[4] Indeed, even when a cancer has developed it will take approximately 3–5 years to develop into a 'late' and likely incurable cancer.[4] Staging in CRC is described using the tumour/node/metastasis (TNM) and Dukes' classification systems outlined in Figure 2.

Once a cancer is established, survival is dependent upon the stage of the disease – as outlined in Table 1. The later the stage, the poorer the prognosis[2] therefore early detection of disease will directly influence patient outcomes.

Risk factors for the development of CRC

The majority of CRC are 'sporadic' – that is, mutations occur by chance. Approximately 15–30% of CRC are 'familial' with no identifiable inherited causative mutation but a clear clustering of cases within a family. It is defined by the presence of two or more members of a family with a family history of adenomatous polyps or CRC.[5] The 'risk' of developing colonic cancer based on family history without identification of any hereditary conditions can be classified as 'high-moderate' and 'low-moderate' (Box 1). It has implications for the commencement and timing intervals of subsequent surveillance.

'Hereditary' CRC represents a group of conditions in which a specific inherited mutation is identifiable. These account for approximately 5% of cases and include familial adenomatous polyposis (FAP), hereditary non-polyposis colorectal cancer (HNPCC), MUTYH-associated polyposis, Peutz-Jeghers syndrome (PJS) and juvenile polyposis syndrome (JPS).[5]

FAP is an autosomal dominant syndrome with an inherited mutation of the APC gene predisposing to the development of 100s to 1000s of adenomatous polyps. HNPCC is caused by mutations of mismatch repair (MMR) genes therefore predisposing the body to the development of multiple cancers. MUTYH-associated polyposis is due to bi-allelic mutations in the base excision repair (BER) gene MUTYH. This is inherited in an autosomal recessive fashion producing multiple adenomatous or mixed adenomatous/hyperplastic polyps. PJS is an autosomal dominant syndrome with inactivating mutations identified in the gene STK11 leading to the development of multiple hamartomatous polyps of the small intestine, colon and rectum with mucocutaneous pigmentation. JPS is characterized by mutations in the SMAD4 gene and BMPR1 signalling pathway. This leads to the development of multiple haematogenous polyps of the colon and rectum.[5]

Aside from genetic predisposition, other risk factors for developing CRC include alcohol use, smoking, obesity, inactivity, diabetes and eating a diet high in red or processed meat. Patients with longstanding colitis are at a higher risk of developing CRC with a cumulative incidence of CRC or dysplasia of 7.7% at 20 years and15.8% at 30 years following onset of colitis.[5] Again these patients can be subclassified into high, intermediate and low risk groups (Table 2) which affect their subsequent surveillance.

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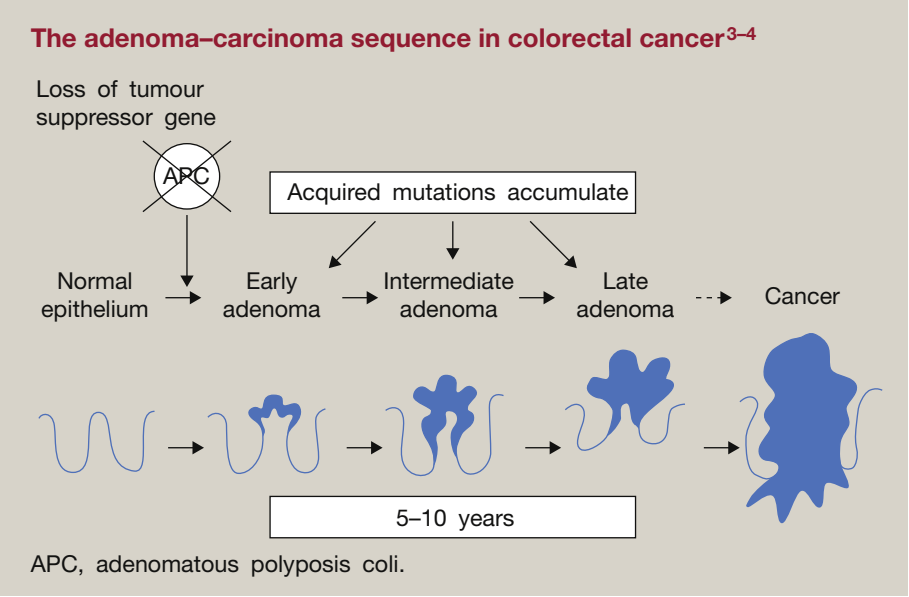

Figure 1

Guaiac-faecal occult blood testing (gFOBt)– rationale and sensitivity

Normally 0.5–1.5 ml of blood is found in the stool per day. It is has been proposed that polyps and cancers will produce an increased microscopic blood loss into the gut lumen due to their friable nature. Detection of this would allow identification of 'at risk' individuals and allow for selective referral for a screening colonoscopy. Haem in the stool contains a pseudoperoxidase; when exposed to hydrogen peroxide, the pseudoperoxidase releases oxygen which in gFOBt converts the guaiac reagent to a blue colour, giving a 'positive' result.

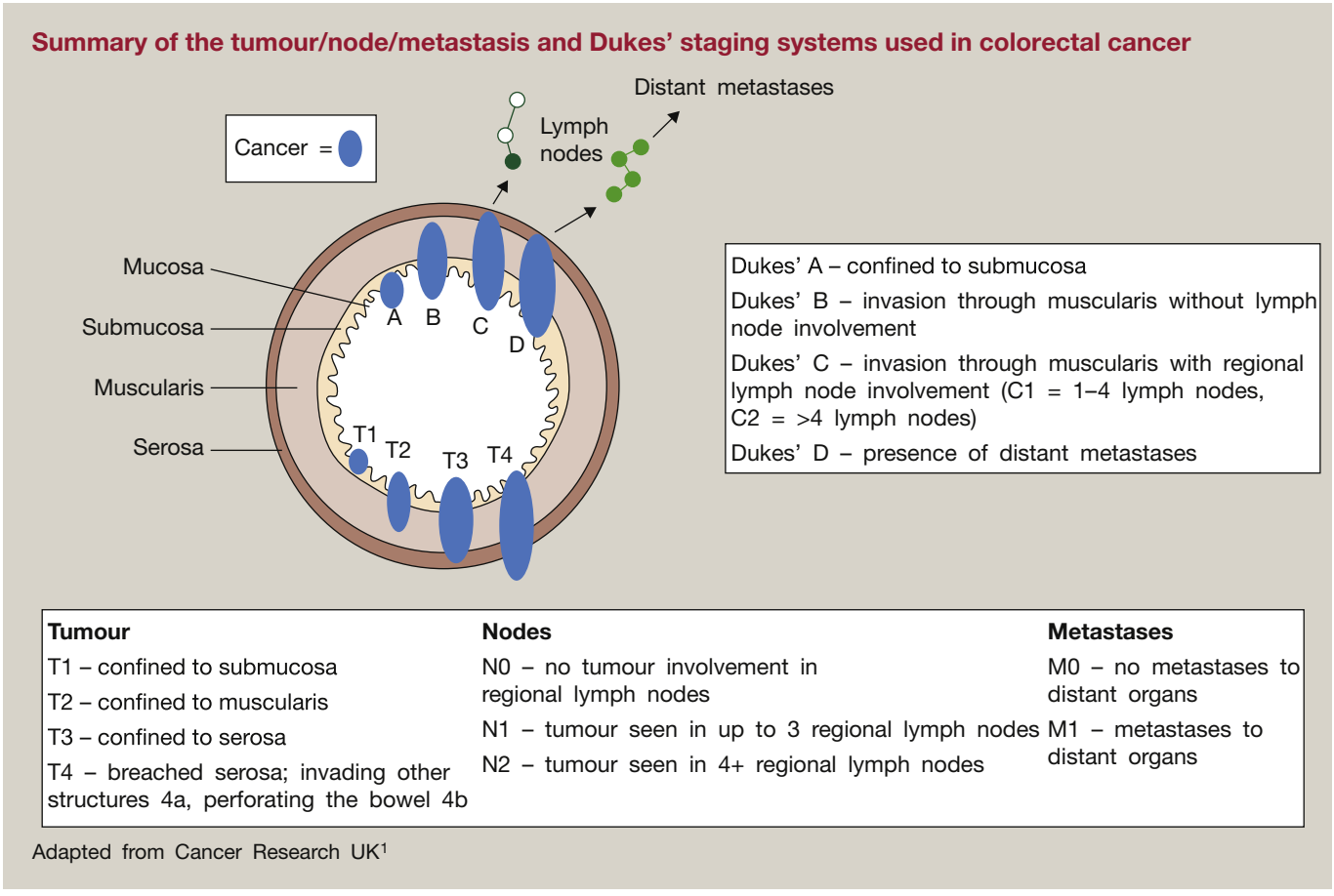

Figure 2