Role of CT colonography for primary colorectal cancer screening

ALISON CORR, ANU OBARO AND DAVID BURLING

Screening for colorectal cancer was introduced in the UK in 2007. It is proving effective, but uptake is relatively low in some parts of the country. In this article the authors describe the rationale behind screening and discuss the potential role for CT colonography as a screening tool.

Colorectal cancer kills more non-smoking adults than any other cancer, affecting 1 in 14 men and 1 in 19 women over their lifetime. 1.5 million people were diagnosed with colorectal cancer worldwide in 2012, and 41 000 in the UK alone. While colorectal cancer can affect young adults in their teens, incidence rises sharply in the over-fifties. Consequently, people are encouraged to participate in colorectal cancer screening programmes from age 50 years in developed countries across the world, including the USA, Japan and Scotland.

The incidence of colorectal cancer has increased slowly in Europe over several decades (particularly in men), with a spike in numbers due to increased detection by the introduction of screening programmes. The UK’s bowel cancer screening programme, for example, was introduced in 2007, with a corresponding sharp rise in cancer incidence, followed by a fall by 2012. It is predicted this trend will continue to fall below pre-screening rates.

Despite screening, five-year survival from colorectal cancer is low in the UK, and compares poorly with most European countries. This is most likely due to delayed clinical presentation, with 25% of people harbouring colorectal cancer presenting with metastatic disease at time of diagnosis.

IS COLORECTAL CANCER THE RIGHT DISEASE FOR SCREENING?

Colorectal cancer is no longer considered to be a single disease but a group of cancers arising from either germline gene mutations (affecting every cell from birth) or acquired somatic genetic mutations (epigenetic effects). However, most colorectal cancer is sporadic and 85% of cancers develop as part of a predictable adenoma–carcinoma pathway, whereby benign adenomatous polyps will typically enlarge over 5 to 10 years and transform from advanced polyp (diameter 10mm+, cell dysplasia or villous histology) into cancer by acquiring genetic mutations. Consequently, for people with polyps destined to grow, there is a ‘window of opportunity’ of several years for polyp detection and removal prior to a malignant transformation.

With the advanced polyp as the target of screening, an interval of five years between tests is frequently recommended. When all advanced polyps are removed, the risk of developing colorectal cancer is virtually eliminated, and the disease can be considered as preventable.

Screening of the whole population is frequently targeted towards detection of early cancer to improve prognosis and
reduce disease specific mortality. While laudable, the time lag between early and late presentation of cancer is relatively short, thus requiring narrower time intervals between tests (for example annual or biennial faecal occult blood testing).

**WHICH TEST FOR SCREENING?**
The vast majority of people (95%) who are screened for colorectal cancer or its precursor (advanced colonic polyp) have no colonic abnormality, thus shifting the rationale for choice of screening test towards less invasive methods of cancer or polyp detection.

The English Bowel Cancer Screening Programme (BCSP) was introduced in 2007 with a primary target of early cancer. The BCSP invites people for biennial faecal occult blood testing (FOBT) between the ages of 60 and 74 years. This approach is evidence-based, leading to a significant (15%) reduction in mortality, with large-scale population pilot schemes supporting its introduction.

More recently, the introduction of ‘one off’ flexible sigmoidoscopy at age 55 years has been shown to decrease cancer incidence by 23% and mortality by 31%. To date, BCSP has tested well over one million people and is predicted to save 2000 lives per year by 2025.

Screening in the USA and some European countries (e.g. Netherlands, Italy) generally utilises colonoscopy or CT colonography (CTC) for direct examination of the whole colon and targeting advanced colonic polyps (to prevent cancer). Despite the benefit of participating in a colorectal cancer screening program, uptake in the UK remains relatively low, with marked regional variation between 42% and 66% (compared to 72% and 79% for breast and cervical screening respectively). In an early pilot study of the BCSP, participation was significantly lower in men than women (47.7% versus 56.1%).

With this in mind, a recent randomised controlled trial of screening from the Netherlands highlighted the impact of uptake on a programme’s effectiveness, with superior uptake for CTC compared to colonoscopy (34% versus 22% \( p=0.0001 \)), improving the overall effectiveness of screening when CTC is the preferred test. The BCSP will only offer colonoscopy or CTC if people test positive to a FOBT, primarily due to insufficient financial resource and capacity. However, primary screening by CTC or colonoscopy is accessible via the independent healthcare sector.

Colonoscopy is a well-established, accurate method of reviewing the colon, which enables polyp removal or biopsy at the same time as examination. However, colonoscopy is relatively invasive and requires careful manipulation of an endoscope throughout the whole colon, necessitating use of sedation in many patients. CTC is a less invasive, less expensive, more convenient alternative.

**WHAT IS CT COLONOSCOPY?**
CTC was first described in 1994 and is now established in routine clinical practice across the UK and in many countries around the world. CTC has several advantages over colonoscopy; use of a thin, short, flexible rectal catheter; reduced laxative bowel preparation; no sedation; better safety profile (no reported deaths); review of extra-colonic organs (detection of early aortic aneurysm or cancer in other organs); decreased cost and improved efficiency.

CTC involves insufflation of the prepared colorectum by carbon dioxide via a small rectal catheter, followed by CT examination of the abdomen and pelvis with the patient in two positions (supine and prone, or on their side if reduced mobility/large BMI). CT scan data is reviewed with 3D computer software, which displays the simulated passage of an endoscope – hence ‘virtual colonoscopy’. These images can be reviewed offline with interrogation of the entire colonic and appendiceal mucosa (Figure 1 and 2).

CTC detects significant colonic polyps in approximately 1 in 15 people, enabling a planned colonoscopic assessment for polypectomy or biopsy. CTC will also identify significant abnormalities outside the colon in approximately 10% of people, including cancer of other abdomino-pelvic organs and aortic aneurysm. The large majority of CTC studies (85%+) will not recommend further investigation and patients are invited to attend for reassessment after a five-year interval.

Currently the quality of CTC examination and interpretation are highly variable, with more experienced centres and radiologists outperforming those who are less experienced. The accuracy of CTC in experienced centres is comparable to colonoscopy in average risk populations >65 years and meta-analysis data comparing the >50 year population.
The largest randomised multi-centre study of CTC performance (SIGGAR trial) recruited more than 4500 patients and found CTC was as accurate as colonoscopy for detection of large polyps and cancer, with superior examination completion rates. However, asymptomatic people in screening populations generally harbour smaller, more subtle cancers and polyps, demanding higher quality technique and interpretation. Consequently, structured training and accreditation programs (similar to those used for colonoscopy) are necessary to ensure safety and limit performance gaps between centres.

**SUMMARY**
Transformation from benign colonic polyp to colorectal cancer is predictable over several years and can be largely prevented by people having a screening test. While the BCSP has a proven track record in reducing colorectal cancer mortality, individuals may choose to undergo more accurate whole colon examination with CTC or colonoscopy. CTC appears to be an optimal screening test, with superior uptake when adopted in a screening programme. However, cancer and its precursor polyp are more difficult to detect in asymptomatic patients, mandating that centres are able to demonstrate excellent CTC performance prior to engagement in colorectal cancer screening.

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**REFERENCES**

**KEY POINTS**
- Colorectal cancer kills more non-smoking adults than any other cancer
- Five-year survival from colorectal cancer is low in the UK, and compares poorly with most European countries
- The Bowel Cancer Screening Programme has now tested over one million people and is predicted to save 2000 lives per year by 2025
- Uptake of screening is relatively low, particularly in men
- Screening with colonoscopy or CT colonography is a potential option
- CT colonography is less invasive and may improve uptake