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[Intervention Review]

# Strategies for detecting colon cancer in patients with inflammatory bowel disease

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#### **ABSTRACT**

#### **Background**

Patients with longstanding ulcerative colitis and colonic Crohn's disease have an increased risk of colorectal cancer (CRC) compared with the general population. This review assessed the evidence that endoscopic surveillance may prolong life by allowing earlier detection of CRC or its pre-cursor lesion, dysplasia, in patients with inflammatory bowel disease (IBD).

# **Objectives**

To assess the effectiveness of cancer surveillance programs for diagnosis of IBD-associated colorectal cancer and in reducing the mortality rate from colorectal cancer in patients with IBD.

#### Search methods

We searched MEDLINE, EMBASE, CENTRAL and clinical clinical trials.gov from inception to 19 September 2016. We also searched conference abstracts and reference lists to identify additional studies.

## **Selection criteria**

Potentially relevant articles were reviewed independently and unblinded by two authors to determine eligibility. Randomised controlled trials (RCTs) or observational studies (cohort or case control) assessing any form of endoscopic surveillance aimed at early detection of CRC were considered for inclusion. Studies had to have a no surveillance comparison group to be eligible for inclusion.

# **Data collection and analysis**

Eligible studies were reviewed in duplicate and the results of the primary research trials were independently extracted by two authors. The primary outcome was detection of CRC. Secondary outcomes included death from CRC, time to cancer detection, time to death and adverse events. Deaths from CRC were derived from life tables, survival curves or where possible, by calculating life tables from the data provided. The presence of significant heterogeneity among studies was tested by the chi-square test. Because this is a relatively insensitive test, a P value of less than 0.1 was considered statistically significant. Provided statistical heterogeneity was not present, the fixed effects model was used for the pooling of data. The 2x2 tables were combined into a summary test statistic using the pooled odds ratio (OR) and 95% confidence intervals as described by Cochrane and Mantel and Haenszel. The methodological quality of the included studies was assessed using the Newcastle-Ottawa scale for non-randomised studies The overall quality of the evidence supporting the primary and selected secondary outcomes was assessed using the GRADE criteria.



#### **Main results**

No RCTs were identified. Five observational studies (N = 7199) met the inclusion criteria. The studies scored well on the Newcastle-Ottawa scale, but due to the nature of observational studies, a high risk of bias was assigned to all the studies. Three studies were pooled to assess the rate of cancer detected in the surveillance group compared to the non-surveillance group. The studies found a significantly higher rate of cancer detection in the non surveillance group compared to the surveillance group. CRC was detected in 1.83% (53/2895) of patients in the surveillance group compared to 3.17% (135/4256) of patients in the non-surveillance group (OR 0.58, 95% CI 0.42 to 0.80; P = 0.0009). Four studies were pooled to assess the death rate associated with CRC in patients who underwent surveillance compared to patients who did not undergo surveillance. There was a significantly lower death rate associated with CRC in the surveillance group compared to the non-surveillance group. Eight per cent (15/176) of patients in the surveillance group died from CRC compared to 22% (79/354) of patients in the non-surveillance group (OR 0.36, 95% CI 0.19 to 0.69, P=0.002). Data were pooled from two studies to examine the rate of early stage versus late stage colorectal cancer (Duke stages A & B compared to Duke stages C & D) in patients who underwent surveillance compared to patients who do not undergo surveillance. A significantly higher rate of early stage CRC (Duke A & B) was detected in the surveillance group compared to the non-surveillance group. Sixteen per cent (17/110) of patients in the surveillance group had early stage CRC compared to 8% (9/117) of patients in the non-surveillance group (OR 5.40, 95% CI 1.51 to 19.30; P = 0.009). A higher rate of late stage CRC (Duke C & D) was observed in the non-surveillance group compared to the surveillance group. Nine per cent (10/110) of patients in the surveillance group had late stage CRC compared to 16% (19/117) of patients in the non-surveillance group (OR 0.46, 95% CI 0.08 to 2.51; P = 0.37). A GRADE analysis indicated that the quality of the data was very low for all of these outcomes. The included studies did not report on the other pre-specified outcomes including time to cancer detection, time to death and adverse events.

#### **Authors' conclusions**

The current data suggest that colonoscopic surveillance in IBD may reduce the development of both CRC and the rate of CRC-associated death through early detection, although the quality of the evidence is very low. The detection of earlier stage CRC in the surveillance group may explain some of the survival benefit observed. RCTs assessing the efficacy of endoscopic surveillance in people with IBD are unlikely to be undertaken due to ethical considerations.

#### PLAIN LANGUAGE SUMMARY

## Strategies for detecting colon cancer in patients with inflammatory bowel disease

# What is inflammatory bowel disease?

Inflammatory bowel disease (IBD) is composed of two main disorders Crohn's disease (CD) and ulcerative colitis (UC). These diseases are chronic inflammatory disorder of the gastrointestinal tract. Common symptoms may include abdominal pain, cramping, diarrhoea, and blood in stools. People with CD may also experience intestinal strictures (a narrowing of a section of the intestine that causes problems by slowing or blocking the movement of food), abscesses (a collection of pus that has built up within the tissue) and fistulae (an abnormal channel or passageway connecting one internal organ to another, or to the outside surface of the body).

#### What is colon cancer?

Long term inflammation associated with IBD leads to an increased risk of colon cancer compared to the risk in people without IBD. Colon cancer is a malignant tumour arising from the inner wall of the large intestine (the colon).

#### What is endoscopic surveillance?

An endoscopy is a non-surgical procedure used to view the digestive tract using a camera. The doctor who performs the endoscopy can take tissue samples of suspicious lesions or growths during the procedure. Endoscopic surveillance is used to identify pre-cancerous growths (called dysplasia) or colon cancer in patients with IBD. Endoscopy may help to identify colon cancer at an earlier stage and help prolong survival and lower the death rate due to colon cancer

# What did the researchers investigate?

The researchers reviewed published studies comparing people with IBD who had endoscopic surveillance to people who did not have endoscopic surveillance to see whether surveillance provided any benefit in terms of diagnosing colon cancer at an earlier stage or reducing the death rate due to colon cancer. The medical literature was searched and analysed up to 19 September 2016.

#### What did the researchers find?

Five observational studies with 7199 patients were used to compare endoscopic surveillance to non-surveillance. The key findings of the review were that a higher rate of cancer occurred in the non-surveillance group compared to the surveillance group, and that a lower rate of colon cancer-associated death was demonstrated in the surveillance group compared to the non-surveillance group. In patients undergoing surveillance, the odds of colon cancer development were reduced by 42% and the odds of death associated with colon cancer was reduced by 64%. Surveillance resulted in detection of a higher rate of early stage colorectal cancer in the surveillance group compared to the non surveillance group which may explain the improved survival seen with surveillance. The overall quality of the evidence is very



low due to the nature of observation studies and the low number of events. Nonetheless, these results suggest that endoscopic surveillance in people with IBD may reduce the development of colon cancer through early detection and may also reduce the chances of dying from colon cancer.