

Cohort study

Long-term follow-up after removal of colorectal adenomas provides evidence for risk stratification of patients at colonoscopic polypectomy

10.1136/ebmed-2014-110110

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Commentary on: Loberg M, Kalager M, Holme O, *et al.* Long-term colorectal-cancer mortality after adenoma removal. *N Engl J Med* 2014;371:799–807.

Context

The association of colorectal cancer (CRC) with pre-existing adenomatous polyps was challenged for decades until the National Polyp Study (NPS) demonstrated that colonoscopic polypectomy prevented deaths from CRC.¹ In a follow-up of the Minnesota Colon Cancer Control study (46 551 participants), those randomly assigned to annual screening with a sensitive faecal occult blood test, sustained a 32% CRC mortality reduction over 30 years which was consistent with the effect of polypectomy.² In the Nurses' Health Study and the Health Professional Follow-up Study (88 902 participants followed over 22 years), lower endoscopy was associated with a 43% CRC mortality reduction compared to no endoscopy.³

Methods

Loberg and colleagues reported a study in which they linked the Norwegian Cancer Registry and the Cause of Death Registry to estimate the cause of death in 40 826 patients in whom colorectal adenomas were removed compared to what was expected in the general population. Standardised mortality ratios (SMR) were calculated comparing expected to observed deaths.

Findings

During a median of 7.7 years of follow-up, no CRC mortality reduction in the entire cohort (SMR 0.96, 95% CI 0.87 to 1.06) was observed. However, Loberg and colleagues did observe a mortality reduction in those with low-risk adenomas (SMR 0.75, 95% CI 0.63 to 0.88) but not in those with high-risk adenomas (SMR 1.16, 95% CI 1.02 to 1.31).

Commentary

In contrast to this study, the NPS cohort, which consisted of 55% high-risk adenoma participants, observed a 53% mortality reduction compared to the US general population. The term 'high-risk adenomas' (advanced adenomas in other studies) has usually been applied to adenomas that have high-grade dysplasia, or are ≥ 1 cm in size, or have $\geq 25\%$ villous

components, or are ≥ 3 in number. 'Low-risk adenomas' (non-advanced adenomas) have none of these features. There is evidence that the risk for future high-risk adenomas and CRC is higher in patients having high-risk adenomas at initial colonoscopy. Most guidelines recommend stratifying postpolypectomy patients into low and high risk for longer (5–10 years) or shorter (3 years) surveillance intervals.⁴

There are several possible explanations for the lack of CRC mortality reduction observed by Loberg and colleagues in patients with high-risk adenomas. Future CRC risk correlates with the initial colonoscopy quality benchmarks including: the rate of caecal intubation, adenoma detection rate, cleansing thoroughness and mean withdrawal time. Completeness of polypectomy, especially of large (high risk) adenomas that are often removed 'piece-meal', is also important to minimise subsequent (interval) CRC. Approximately 70% of interval CRC's are a result of either missed lesions or incomplete polypectomy.⁴ It would be of interest if the authors could link their mortality data to colonoscopy performance. This information was not included in the paper. Although not assessed by Loberg, we could make the assumption that polypectomy converted their initially high-risk group to a general population average risk group.

The added benefit of surveillance to the initial colonoscopy was not determined in the study since the cohort did not reach the time threshold for surveillance (median follow 7.7 years; first surveillance in Norway recommended in 10 years). In contrast, the NPS cohort had several surveillance colonoscopies. The relative effect of surveillance compared to the baseline colonoscopy needs further study in patients with high-risk and low-risk adenomas.

Implications for practice

The study provides evidence for the high subsequent CRC risk in patients with high-risk adenomas at baseline. Other studies have demonstrated a CRC mortality reduction in this group, which supports the current recommendation in guidelines for their intense surveillance. Loberg and colleagues' observations of a CRC mortality reduction in the low-risk adenoma subset provides evidence that this group has a low future CRC risk requiring little or no surveillance.

Emphasis on high-quality examinations at each step and strict adherence to surveillance guidelines, especially in patients with low-risk adenoma, can reduce the financial burden, medical resource drain and human cost in achieving our common goal of reducing deaths from CRC.

Competing interests None.

Provenance and peer review Commissioned; internally peer reviewed.



References

1. Zauber AG, Winawer SJ, O'Brien MJ, *et al.* Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med* 2012;366:687–96.
2. Shaumat A, Mongin SJ, Geisser MS, *et al.* Long-term mortality after screening for colorectal cancer. *N Engl J Med* 2013;369:1106–14.
3. Nishihara R, Wu K, Lochhead P, *et al.* Long-term colorectal-cancer incidence and mortality after lower endoscopy. *N Engl J Med* 2013;369:1095–105.
4. Lieberman DA, Rex DK, Winawer SJ, *et al.* Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2012;143:844–57.