

Long-Term Success of Endoscopic Polypectomy in Reducing CRC Incidence

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Because most colorectal cancers (CRC) arise from adenomas, it is reasonable to expect a substantial reduction in CRC incidence from endoscopic polypectomy and subsequent surveillance. There is considerable evidence to support this. The Minnesota Colon Cancer Control Study, a randomized controlled trial to evaluate Hemoccult screening, found significant 20% and 17% reductions in colorectal cancer incidence in the annual and biennial screened groups respectively after 18 years of follow-up (Mandel et al. 2000). The reduction was believed to be due to the identification and removal of adenomas, although direct evidence was lacking. These findings were based on a standard intent to treat analysis even though most members of the screening groups did not have a positive screen throughout the trial. Church et al., in a subsequent preliminary analysis of the data to estimate the effect of polyp removal in individuals whose polyps were detected (ie, the true reduction in CRC incidence), found that the estimated incidence reduction among those with an adenoma was about 68%, 73% in women and 67% in men (Church et al, 2005 personal communication). The confidence interval around this effect is consistent with the results from the National Polyp Study (Winawer et al, 1993) and from the study by Newcomb et al (Newcomb et al, 2003). These studies suggest that the potential reduction in CRC incidence from endoscopic polypectomy is substantial.

Counterbalancing these results are two European trials of Hemoccult screening that found similar incidence rates for the screened and control groups (1.49 and 1.44 per 1000 population in the Nottingham trial and 1.71 and 1.72 per 1000 population in the Funen trial) (Hardcastle et al. 1996; Kronberg et al. 1996). After 19 years of follow-up in the Nottingham trial, the incidence rates were higher, but still similar for control and screened groups (1.53 v. 1.51 per 1000 population; $p=0.76$) (Scholefield et al. 2002). Complicating the interpretation of this finding is the fact that in the early years of the study the screened group had a slightly higher incidence of CRC than the control group. The cumulative incidence curves crossed at 8 years and have remained separated. Noteworthy is the fact that the cumulative colonoscopy rate in this trial was only 1.9% of the intervention group so the expected reduction in incidence would not be very large. In the Funen trial, 4.3% of those screened or about 2% of the entire group assigned to screening received a colonoscopy. Therefore, the results from these two European trials might not be at odds with the studies above given the relatively low rates of colonoscopy.

Panel 2.2

Three adenoma chemoprevention trials (ACTs) provide an opportunity to address the issue of CRC incidence following polypectomy. In these trials, patients with at least one adenoma were randomly assigned to an intervention (eg. antioxidants, calcium, aspirin) or placebo group. They underwent colonoscopy, typically 3 to 5 years later, to ascertain recurrent adenomas, the primary endpoint in the trials. In addition, all study participants were followed to ascertain cancer incidence (1.8 per 1000 person-years) and the expected number of cases was obtained by applying SEER incidence rates to person-years at risk. The observed to expected incidence of CRC was 0.98 (95% CI: 0.63-1.54) (Robertson et al, In press). Although no difference was observed, it is reasonable to expect that the study population was at higher risk to begin with because all participants had at least one adenoma. Overall, 30% had at least one adenoma greater than 1 cm. at the qualifying examination and 25% had a history of adenomas prior to this exam. Therefore, an SIR of 0.98 may actually represent a fairly large reduction.

The rate of 1.8 per 1000 person-years (py) noted above was somewhat lower than the rates reported for the Polyp Prevention Trial (2.2/1000 py), The Wheat Bran Fiber Trial (2.4/1000 py) and the Funen Adenoma Study (2.2/1000 py). These are in contrast to the National Polyp Study where the CRC incidence rate was 0.6/1000 py, a rate more similar to that reported in an Italian study (0.4/1000 py) (Citarda et al. 2001). The differences among these trials in CRC incidence rates might be due, in part, to the age and gender distributions of the study participants and the percentage of study participants undergoing follow-up colonoscopy (97% in the ACTs, 80% in National Polyp Study and 74% in Italian study) and the benefit from two of the interventions in the ACTs, calcium and aspirin. The higher rate of colonoscopy could result in detecting asymptomatic lesions and the effective interventions may have reduced the incidence of CRC. In addition, in the ACTs the relatively high rate of CRC (4/1000 py) at the year one colonoscopy examination relative to the rate in the subsequent three year period (1/1000py) suggests that prevalent cancers may have been missed at the baseline exam.

Despite differences in results among the studies, most of which can be explained, it remains reasonable to conclude that endoscopic polypectomy leads to a reduction in CRC incidence. The magnitude of the effect is probably less than 90% but still substantial.