EDITORIAL

Colon-Polyp Surveillance — Do Patients Benefit?

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In March 2014, newspaper headlines trumpeted the stunning reduction in mortality from colorectal cancer of 30% from 2000 to 2010 in the United States.[1] There were also significant reductions in colorectal-cancer incidence. Some of this reduction is due to colonoscopic detection and removal of adenomas.[2,3] Patients in whom adenomas develop remain at risk (owing to genetics or lifestyle) for the discovery of adenomas on subsequent examinations, leading to the logical rationale for surveillance colonoscopy in adenoma-bearing patients.[4]

Colon-polyp surveillance now accounts for about 25% of colonoscopies among persons over 50 years of age in the United States, a substantial burden on health resources.[5] Therefore, it may come as a shock that evidence is lacking that polyp surveillance reduces colorectal-cancer incidence or mortality. It is quite possible that the initial colonoscopy and polypectomy reduce the risk of death from colorectal cancer and that surveillance may have little additional effect on mortality.

Most studies of surveillance do not have colorectal-cancer incidence or mortality as an end point. The polyp-surveillance guidelines are based largely on studies that use high-risk adenomas as a surrogate for colorectal cancer, and this surrogate is not perfect.[4] These studies have differentiated between patients with high-risk and those with low-risk adenomas. The evidence suggests that patients with high-risk adenomas (defined as a tubular adenoma ≥10 mm in diameter, an adenoma with villous histologic features or high-grade dysplasia, or three or more adenomas) at the baseline colonoscopy have a higher likelihood of having high-risk adenomas during a follow-up colonoscopy than do persons with no polyps or low-risk adenomas (defined as one or two tubular adenomas <10 mm in diameter) at baseline. Presumably, patients with high-risk adenomas are also at risk for colorectal cancer, and practice guidelines recommend intensive colonoscopic surveillance at 3-year intervals. Patients who have undergone resection of low-risk adenomas are at lower risk for the development of high-risk adenomas, and current guidelines recommend surveillance at a longer interval, of 5 to 10 years, depending on the quality of the baseline examination. Missing are data about colorectal-cancer incidence and mortality after the removal of high-risk and low-risk adenomas.

The study from Løberg et al.[6] in this issue of the *Journal* uses population-based data from a cancer registry in Norway that includes cancers and adenomas reported since 1993. Since there is no organized screening in Norway, we presume that most colonoscopies were performed to evaluate symptoms. In addition, most patients would not receive surveillance before 10 years after resection of adenomas, on the basis of Norwegian guidelines. These practices differ from those in the United States but are still informative about the outcome in patients with adenomas. The authors use unconventional definitions of high-risk and low-risk adenomas because they lacked data on polyp size and the precise number of polyps. For this analysis, low risk was defined as the presence of one tubular adenoma (any size), and high risk was defined as the presence of two or more adenomas or any adenoma with villous histologic features or high-grade dysplasia. During a mean follow-up of 7.7 years after initial colonoscopy and polypectomy, patients with a low-risk adenoma had a 25% lower risk of death from colorectal cancer than expected rates in the general population. If we assume that patients with adenomas might have a higher risk of colorectal cancer relative to the general population, then this lower risk sug-

gests that detection and removal of a single adenoma identifies a person who is at very low risk. Surveillance colonoscopy in such patients may produce more harm than benefit. Despite the unconventional definition of a "low-risk adenoma," these data support the notion that colonoscopy may identify patients who have a low risk of death from colorectal cancer and who may not need any surveillance.

What about the patients with high-risk adenomas? This new study shows that despite polypectomy, colorectal-cancer mortality among such patients is higher than that in the general population (standardized mortality ratio, 1.16; 95% confidence interval, 1.02 to 1.31). There are several possible reasons for this important finding. Patients with high-risk adenomas may have other lesions that were missed at the baseline colonoscopy. In an analysis of interval cancers pooled from eight studies, missed lesions most likely accounted for more than 50% of the interval cancers that were found within 3 to 5 years after the baseline examination.[7] A second explanation is the possibility that polyps were detected but incompletely removed at baseline. Residual neoplastic tissue, particularly that with high-risk histologic features (villous features or high-grade dysplasia), might progress to colorectal cancer. This may occur in more than 10% of polypectomies,[8] despite careful attempts at complete resection. These two factors are directly related to the quality of the colonoscopy. A third possible explanation is that colorectal cancer may be more likely to develop in persons with high-risk adenomas because of genetic or lifestyle predisposition.

Whether the results in the current study are due to missed lesions, incompletely removed lesions, or new lesions, this study provides evidence of higher colorectal-cancer mortality in patients with high-risk adenomas. Colorectal-cancer incidence and mortality among patients with high-risk adenomas is probably diluted by including patients with two small tubular adenomas, which are considered low-risk adenomas in most other studies. If these patients were not included in the group with high-risk adenomas, incidence and mortality might even be higher. We are missing important information about the quality of colonoscopy in Norway, which could have contributed to the outcomes, particularly in the high-risk group. Nevertheless, Løberg et al. provide justification for surveillance in patients with high-risk adenomas.

The goals of colonoscopic surveillance in patients with adenomas are to prevent interval cancers and reduce colorectal-cancer mortality. The study by Løberg et al. does not prove that intense surveillance in patients with high-risk adenomas would necessarily achieve these goals, but it does show that this is a cohort at risk for colorectal cancer after colonoscopy. Future study will be needed to prove that surveillance actually achieves the desired goals. Conversely, the authors show that we might be able to identify a low-risk group. In the United States and abroad, there is now recognition that colonoscopic quality is variable and that poor quality is associated with higher rates of interval colorectal cancer.[9] If high-quality colonoscopy is performed, meaning excellent detection and complete removal of polyps, surveillance may not be needed for most patients with low-risk adenomas. If future studies, which include information about the quality of the examination, confirm that patients with low-risk adenomas would not benefit from surveillance, this would be an exciting development for patients and health care systems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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