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Smoking and the Increased Risk for Serrated Polyps

Implications for Screening and Surveillance

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EDITORIAL

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• REFERENCES

Identifying risk factors that can predict which individuals are at risk for colorectal neoplasia can be used to screen for colorectal cancer (CRC) more efficiently. Assigning numerical values, that are based on results from models, to these factors can help stratify individuals into high and low-risk groups. One potential strategy could involve adults with high-risk scores receiving more sensitive but more invasive tests such as colonoscopy, while those in the low-risk group undergo fecal immunochemical test (FIT) testing. In the current paper, the authors examine an important colorectal neoplasia risk factor, smoking and its association with colorectal neoplasia.¹

Using a case-control design, the investigators examined data from 828 consecutive participants and compared the risk factors in adults with adenomas and serrated polyps with those in adults without any polyps. Smoking exposure was quantified by status, duration, and intensity. They also examined other important risk factors such as sex, ethnicity, alcohol use,² obesity,³ physical activity, family history of CRC, and medication use. After adjusting for the covariates, they observed that current smoking was strongly associated with conventional adenomas [odds ratio (OR)=3.01; 95% confidence interval (CI): 1.90-4.74]. In addition, smoking >20 years had a similar increase in risk (OR=2.98; 95% CI: 1.85-4.79), as compared with nonsmokers or those who had smoked for <1 year. They also observed that smoking >20 pack years was significantly associated with having serrated polyps (OR=5.91; 95% CI: 2.64-13.22). Of note, the point estimate for the risk for serrated polyps was higher than that for conventional adenoma, suggesting a stronger link between tobacco exposure and serrated polyps. However, the 95% CIs for the 2 risks overlapped. Overall, the findings of the study suggest that smokers with a 20-year or greater exposure had an elevated risk for conventional adenomas as well as several polyps.

These data support the findings of a meta-analysis based on data from several screening studies⁴⁻⁶ that demonstrated that smoking exposure is associated with a 2-fold increase for colorectal neoplasia.⁷ A threshold exposure of about 20 pack years or greater has been observed in other studies.^{6,8} This exposure level is consistent with the findings of the current study, as the individuals in the current study smoked for an average of 28 years, and the intensity was ~1 pack per day.

The study also demonstrated that serrated polyps were significantly associated with smoking. Smoking has been shown to be associated with the serrated pathway and, in fact, has been linked with even small serrated lesions known as aberrant crypt foci⁹ or abnormalities in the mucosa, which are only a few crypts in size. Smoking has also been linked with having sessile serrated polyps,¹⁰ especially those large lesions on the right side of the colon.¹¹

There are important implications for these data, as serrated polyps are part of a pathway that may account for up to 30% of all CRCs.¹² Serrated polyps are a family of colorectal lesions that include the commonly detected hyperplastic polyps, sessile serrated polyps, and the much less commonly encountered traditional serrated polyps.¹³ Sessile serrated polyps (SSPs) are of the greatest concern for endoscopists, as they can develop dysplasia and thus CRC. In addition, they are flat and can be easily missed. However, as it can be difficult to distinguish between some hyperplastic polyps and SSPs, other factors that are predictive of SSPs, such as larger size and proximal location,¹⁴ may be used to identify clinically significant serrated polyps. An analysis of a screening trial in Europe demonstrated that individuals with large (≥ 1 cm) serrated polyps may be at a similar risk for CRC as those individuals with advanced adenomas on index exam.¹⁵ While the current study did not examine serrated polyps by size or histology, they did analyze by location and observed that smokers were at an ~6-fold increased risk for proximally located serrated polyps. Thus, the current study suggests that smokers are at significantly increased risk for clinically important serrated polyps that might be SSPs.

As smokers appear to be at an increased risk for serrated polyps, the choice for a screening test may be an important consideration. It has been shown that fecal immunochemical testing may not be as sensitive for flat polyps,¹⁶ especially those that are serrated.^{17,18} This is because they tend to bleed less than protruding or conventional adenomas. Conversely, fecal DNA testing may be more sensitive than FIT due to the presence of 2 methylation markers.¹⁹ Thus, the fecal DNA may be a better stool-based test to screen smokers than FIT. In addition, as serrated polyps and other lesions observed in smokers tend to be flat,²⁰ CT colonography may not be an appropriate screening test.²¹ Therefore, colonoscopy that has the best sensitivity for serrated polyps may be the test of choice for smokers (Table 1).

Finding	Potential Implication	Potential Recommendation
Smokers have a higher risk for adenomas	ADR might be higher in a population with smoking	Endoscopists should be cognizant of the risk for NAAP and provide quality colonoscopy. Should ADR be higher in populations with smokers?
Smokers have a higher risk for serrated polyps	FIT may not be the best stool test. TPCK may be a better stool test. CT colonography may be ineffective. Colonoscopy is most sensitive.	Colonoscopy may be the most effective screening test.
Smokers are at elevated risk for synchronous NAAP and conventional adenomas	May be at higher risk for metachronous high-risk conventional adenomas. May be at risk for interval CRC.	Individuals with synchronous adenomas and NAAP may require closer surveillance.

ADR indicates adenoma detection rate; CRC, colorectal cancer; TPCK, stool DNA; FIT, fecal immunochemical test; NAAP, non-adenomatous polyps.

TABLE 1

Smoking may also have an important impact on screening and surveillance with colonoscopy, because their increased risk for adenomas and serrated polyps will allow for higher detection rates.²² Given the importance of achieving adequate adenoma detection rate (ADR) in ensuring protection from interval cancers,²³ adjustment in ADR benchmarks to appropriately account for these factors may be indicated in populations with particularly high prevalence of these risk factors. For example, a population in which 50% of the screening population has a *20-pack-year or greater* smoking exposure, such as those observed in a population such as that of the Veterans Affairs,²⁴ might require a higher ADR to ensure adequate protection from interval CRC. In addition, given the difficulty in detecting serrated polyps, careful attention to quality measures such as adequate bowel preparation and withdrawal time will be crucial in detecting serrated polyps.^{25,26} More recently, a study demonstrated that smoking had a stronger link with individuals who had both clinically significant serrated polyps as well as conventional advanced adenomas, as compared with even those individuals with high-risk adenomas alone.²⁷ This group of individuals with both lesions of the separated and conventional pathway have been shown to have an increased risk for metachronous advanced neoplasia²⁸; thus, smoking may have a significant impact on risk for future lesions as well as index lesions.

Finally, as smoking may increase the risk of individuals for adenomas and serrated polyps, should they be screened at an earlier age? This question is of great concern given the recent reports of an increased prevalence of CRC in adults less than 50 years of age.²⁹ The American College of Gastroenterology 2009 guidelines suggested that smokers who had a 20-pack-year history of smoking should be considered high risk.³⁰ The guidelines fell short of recommending that those individuals with a 20-pack-year history of smoking receive CRC screening at 45 years of age due to lack of data. Thus, more data are needed regarding the age at which smokers should start screening and which tests are the most effective in this population.

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