Modifiable Risk Factors for Esophageal Adenocarcinoma in Barrett’s Esophagus

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Esophageal adenocarcinoma (EA), a type of esophageal cancer, has been on the rise over the past four decades. Mortality has also increased during this time, and survival is poor: the majority of patients diagnosed with EA die within 12 months. A pre-cancerous condition called Barrett’s esophagus (BE) occurs in an estimated 10-15% of patients with stomach acid reflux. Although BE patients’ risk of EA is 30 times that of people without BE, it is still not known which persons with BE are most likely to develop EA, or whether certain lifestyle or behavior modifications or medical interventions might help prevent EA within this higher-risk cohort. Previous studies have looked at obesity, cigarette smoking, gastroesophageal reflux and diet as potential modifiable risk factors for EA. Modifiable factors are important from a public health perspective, as they offer the possibility of reducing a patient’s risk of EA and reducing the burden of disease in the population.

Drs. Sheetal Hardikar and Tom Vaughan, together with colleagues in Public Health Sciences and Human Biology, addressed this question, specifically looking at whether smoking, obesity, or alcohol use would predict progression to EA among a cohort of 411 persons with BE from the Seattle Barrett’s Esophagus Study. They estimated hazard ratios (HR; similar to relative risks), accounting for differences in age, gender, and other potentially confounding factors.

Investigators found that among persons with BE, those who were older were at greater risk of progressing to EA, with risk increasing about 3% per year of life (HR 1.03, 95% CI 1.00-1.06). With regard to modifiable risk factors, previous studies have shown that smoking approximately doubles the risk of EA in the general population. In this report, investigators observed an association of similar magnitude among persons already known to have BE. Heavy smokers with BE were more than twice as likely to develop EA as non-smokers with BE (HR 2.29, 95% CI 1.04-5.07) after adjustment for potential confounding factors. With regard to alcohol use, previous studies suggest that alcohol consumption does not increase risk of EA in the general population (even though it is associated with a 10-fold increase in risk of esophageal squamous cell carcinoma, the other major type of esophageal cancer). In the present study, alcohol consumption did not appear to be a risk factor for EA among persons with BE (HR 1.00, 95% CI 0.37-2.69 for more than 3 drinks per day versus none, adjusted for cigarette use and other potential confounding factors).
Finally, there is some evidence from earlier studies that high body mass index (BMI) and abdominal adiposity play a role in the development of EA in the overall population. Abdominal obesity tends to be a more important factor in developing BE than does BMI. In the present study, high BMI was not associated with the progression from BE to EA. Authors noted a suggestion of an association with waist-to-hip circumference ratio (adjusted p-value for trend = 0.12) in men. This finding needs to be confirmed, but if there is indeed an association between abdominal adiposity and progression to EA, it may be explained by the inflammatory effects of adipose tissue, and/or an increase in reflux due to the intra-abdominal pressure exerted by extra abdominal fat.

The observed association with smoking is interesting because it provides clues about the role of smoking in the development of EA: based on this study and earlier ones, smoking appears to play a role in both the development of BE, and in progression from BE to EA, approximately doubling the risk of each. The mechanisms underlying this relationship are unclear. However, in addition to the carcinogenic components of cigarette smoke, and its potential effects on inflammation and proliferation, cigarette smoke is also thought to relax the esophageal sphincter, which could result in reflux. This work could inform future interventions to prevent progression to EA among high-risk persons with BE.


In Barrett’s esophagus, the epithelial cells possess several properties which distinguish them from normal cells. These include the ability to secrete thick mucous (a), and the production of anions, including bicarbonate, at much higher levels than normal esophageal epithelial cells (b).

(Image modified from one provided by author and featured in second reference below)