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No Significant Effects of Smoking or Alcohol Consumption on Risk of Barrett's Esophagus

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Abstract

Background—Smoking, but not higher alcohol consumption, is associated with increased risk of esophageal adenocarcinoma (EAC) and progression from Barrett's esophagus (BE) to EAC. However, it is still unclear whether smoking or alcohol is implicated in the development of BE.

Aim—To evaluate the associations between smoking, alcohol and the risk of BE.

Methods—The study included eligible patients scheduled for elective esophagogastroduodenoscopy (EGD) and a sample of patients eligible for screening colonoscopy recruited from primary care clinics. We compared 258 patients with definitive BE with two separate control groups: 453 patients from the primary care group ("colonoscopy controls") and 1,145 patients from the elective EGD group ("endoscopy controls") with no endoscopic or histopathologic BE. We calculated odds ratios (OR) and 95 % confidence intervals (95 % CI) using multivariable logistic regression models.

Results—Seventy-seven percent of BE cases, 75 % of colonoscopy controls and 72 % of endoscopy controls were ever smokers. Of these, approximately 45 % were current smokers.

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Conflict of interest None.

Overall, 91 % of study participants were ex or current alcohol drinkers, with the majority drinking beer. We found no association between various measure of smoking exposure (status, intensity, age at initiation, duration, pack-years and cessation) and risk of BE. Alcohol consumption was not associated with increased risk of BE. Conversely, moderate intake was associated with lower risk (14 to<28 drinks/week, OR 0.39, 95 % CI 0.15–1.00).

Conclusion—Smoking and alcohol were not strong or consistent risk factors for BE. The likely role of smoking in increasing risk of EAC is through promoting progression from BE to cancer.

Keywords

Alcohol; Barrett's esophagus; Epidemiology; Risk factors; Smoking

Introduction

Barrett's esophagus (BE) is an acquired condition in which specialized columnar epithelium replaces the usual stratified squamous epithelium lining the esophagus. BE is the only known precursor to esophageal adenocarcinoma (EAC) and is associated with an annual risk of progression to cancer of approximately 0.2 % [1–4]. EAC is of great public health importance as its incidence has increased sixfold over the past four decades and rates continue to rise [5, 6]. Moreover, survival for patients with EAC remains poor, with median survival less than 12 months [7]. Understanding the causes of BE is a necessary step toward preventing EAC.

BE affects approximately 2 % of the Western population and is most prevalent in White men aged over 50 years [8]. Potentially modifiable risk factors for BE include gastroesophageal reflux disease (GERD) and abdominal obesity [9, 10], while use of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) may prevent the development of BE [11]. However, the associations between smoking, alcohol and risk of BE remain unclear. If the associations were shown to be causal, then smoking and alcohol would be key targets for early prevention of EAC.

Results from a pooled analysis of 12 studies in the Barrett's and Esophageal Adenocarcinoma Consortium (BEACON) show a consistent association between smoking and risk of EAC. Compared to never smokers, risk among ever smokers was twofold higher and risk increased linearly with increasing pack-years of smoking exposure [12]. However for BE, a pooled analysis of four BEACON studies reported a 67 % increased risk associated with ever smoking but no clear dose–response effect among ever smokers [13]. Importantly, the summary risk estimate from this pooled analysis was affected by significant between-study heterogeneity. While two studies reported an increased risk for ever smokers [14, 15], there was no association in two others [16, 17]. Making causal inferences more difficult, in one of the two studies that reported a significant association between ever smoking and BE, former smokers but not current smokers had significantly higher risk [14]. Furthermore, as studies examining the smoking-EAC association in BE patients [18–20] and the general population [12] have reported similar effect sizes, most of the effect of smoking may actually occur after the development of BE rather than in initiating the development of BE in the first place

Higher alcohol consumption is not associated with increased risk of EAC [21]. Conversely, EAC data from BEACON show an apparent inverse association with beer and wine intake. BE studies have generally reported null findings for alcohol consumption; however results among studies reporting beverage-specific effects have been conflicting [22–25]. While some have reported an inverse association with wine consumption [23–25], others have found lower risk associated with beer [25] and some evidence for higher risk associated with

liquor [22, 24]. These contrasting findings may be due to measurement error; one study captured lifetime alcohol exposure [25], others used recent alcohol exposure which may be affected by disease status in case–control studies [23, 24].

In light of the inconsistent findings to date, additional validation of the associations between smoking, alcohol and BE is necessary. We investigated the effects of multiple dimensions of smoking exposure and different patterns of alcohol consumption on the risk of BE. Using data from a study among US veterans, a high-risk population (mostly older White men) with high smoking rates and alcohol exposure, we aimed to estimate the effects of smoking and alcohol on BE among persons with high levels of exposure.

Methods

Details of the study population and methods have been described in full elsewhere [26]. Briefly, data came from a case–control study of BE conducted at the Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC) in Houston, Texas. The study was approved by the Institutional Review Boards for MEDVAMC and the Baylor College of Medicine.

Study Participants

Study participants were recruited between 15 February 2008 and 14 December 2012 from among consecutive eligible patients undergoing an elective esophagogas-troduodenoscopy (EGD) for any indication, and consecutive patients attending one of seven selected primary care clinics in the Houston VA. The primary care patients were eligible for a screening colonoscopy and agreed to undergo the study EGD during the same clinical visit as their colonoscopy. None of the primary care patients were primarily referred for EGD. The elective EGD and primary care groups combined represent all patients, who, if they had BE, would be diagnosed with BE at the Houston VA (i.e., the source population for BE). The eligibility criteria were: (1) age 50–80 years (40–80 years for the elective EGD group); (2) no previous gastroesophageal surgery; (3) no previous gastroesophageal cancer; (4) no active lung, liver, colon, breast or stomach cancer; (5) no anticoagulants; (6) no significant liver disease indicated by platelet count below 70,000 ascites or known gastroesophageal varices; and (7) no history of major stroke or mental condition.

All study participants underwent a study EGD with systematic recording of suspected BE based on the Prague circumferential and maximum length classification [27] and targeted biopsies from these areas using Jumbo biopsy forceps. BE was defined as the presence of specialized small intestinal epithelium in the histopathological examination of at least one biopsy obtained from endoscopically-suspected BE areas. Patients from the elective EGD group and the primary care group with no suspected or definitive BE served as endoscopy controls and colonoscopy controls, respectively. Among eligible patients in the EGD group, 70 % completed the study (underwent the study EGD and completed the study questionnaire). In the primary care group, 43 % of eligible patients completed the study; however 85 % of patients who underwent their colonoscopy completed the study.

Data Collection

Study participants completed a computer assisted survey before the study EGD. The survey ascertained information about social background, lifetime history and current use of alcohol and cigarette smoking, physical activity, medical history, onset, frequency and severity of heartburn or regurgitation symptoms, and use of H_2-receptor antagonists, proton pump inhibitors (PPIs), non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin. Height and weight were measured prior to the study EGD and were used to calculate body mass index (BMI). A flexible tape measure was used to measure waist and hip circumference. We

defined duration of GERD symptoms as the sum of the duration of at least weekly heartburn or regurgitation symptoms. Participants were defined as *H. pylori* positive if organisms were seen on histopathology of any of the study gastric biopsies. If biopsy results were not available, participants were defined as positive for *H. pylori* if review of the medical record showed a previous positive biopsy, presence of serum antibodies, or treatment received.

We defined ever smokers as those who smoked more than 100 cigarettes, cigars or pipes during their lifetime. Ever smokers included *ex-smokers* who quit smoking at least 1 year prior to the study, and *current smokers* (including those who quit within the previous year). We calculated time since quitting as the difference between the age at which *ex-smokers* had stopped smoking and their age 1 year prior to the study. Smoking intensity was defined as the self-reported average number of cigarettes smoked per day and smoking duration was estimated by subtracting starting age from quitting age for *ex-smokers* and age at study EGD for *current smokers*. Finally, we derived the number of pack-years of cigarette exposure by dividing the number of cigarettes smoked daily by 20 and multiplying by smoking duration.

For alcohol, we asked participants whether they currently drank alcohol, were life-long non-drinkers, or had previously drunk alcohol but stopped. Ever drinkers were then asked if they had consumed alcohol at least monthly for 6 months or more, and if so, to report frequency of consumption for four classes of alcohol (beer, white wine, red wine and liquor/spirits) at ages 20–29, 30–49 and ≥50 years, as applicable. We calculated average lifetime total alcohol consumption (in standard drinks per week) by dividing total alcohol consumption (standard drinks; summed across all age groups for each class of alcohol) by duration of drinking since age 20 years (in weeks). Similar algorithms were used to calculate average lifetime beverage-specific consumptions.

Statistical Analysis

We used never smokers as the reference group for analysis of each cigarette smoking measure. For alcohol, the reference group included those participants who were lifelong non-drinkers. Our study (453 colonoscopy controls and 258 BE cases) had 80 % power to detect an odds ratio (OR) of ≥1.65 for current smoking and current drinking, assuming 35 and 50 % prevalence in the control group, respectively, and at $\alpha = 0.05$. We compared the characteristics of BE cases and controls using Chi square tests for categorical variables and Student's *t* test for continuous variables. ORs and corresponding 95 % confidence intervals (95 % CI) were estimated to assess the associations between cigarette smoking, alcohol consumption and risk of BE using unconditional logistic regression. The multivariable models were adjusted for potential confounders including age, sex, race, duration of GERD symptoms, waist-to-hip ratio (WHR), *H. pylori* infection status, PPI use and NSAID use. We performed tests for trend by assigning the median value to each category of the main exposure and modeling this value as a continuous variable in the regression model. We performed subgroup analyses to examine whether the associations with smoking and alcohol varied across strata of age (<60, ≥60), WHR (low, high; where high WHR cutoff was considered ≥0.9 for males and ≥0.85 for females), duration of GERD symptoms (never, <30 years, ≥30 years), *H. pylori* status (negative, positive) and presence of hiatal hernia (absent, present). Tests for interaction were performed by the Wald test, using interaction terms in the model. Statistical significance was determined at $\alpha = 0.05$ and all tests for statistical significance were two-sided. All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC).

Results

This study included data from 258 patients with BE, 453 colonoscopy controls and 1,145 endoscopy controls. The distributions of study participant characteristics are shown in Table

1. Ninety-two percent of participants were male; however, BE cases were still significantly more likely to be male than endoscopy controls (97.7 vs. 88.7 %). As expected, the proportion of Whites in the BE group was significantly higher than that in the colonoscopy (88.0 vs. 54.7 %) and endoscopy (63.2 %) control groups. Compared to controls, BE cases were more likely to report GERD symptoms and PPI use, and less likely to be infected with *H. pylori*. We found no significant differences in NSAID use or BMI among the three groups, however BE cases had significantly higher average WHR than controls.

Table 2 shows the associations between smoking and BE. Prevalence of ever smoking was highest in BE cases (77 %) followed by colonoscopy controls (75 %) and endoscopy controls (72 %). BE cases had a higher proportion of current smokers (34 %) than colonoscopy controls (30 %), but not endoscopy controls (34 %); however, the differences in these proportions were not statistically significant. In multivariable regression analysis, we found no significant association between smoking status and BE for comparisons with colonoscopy controls or endoscopy controls. Furthermore, while smokers in the BE case group smoked for longer durations and at higher intensity than smokers in the control groups, there were also no significant associations between pack-years of smoking exposure, smoking intensity, or smoking duration and the risk of BE (Table 2). Likewise, we found no statistically significant associations between age at smoking initiation or smoking cessation and BE.

When we restricted our analyses to only White males (222 BE cases, 243 colonoscopy controls and 655 endoscopy controls), we again found no significant association between smoking and BE (for current smokers: BE vs. colonoscopy controls, adjusted OR 1.08, 95 % CI 0.59–1.98; BE vs. endoscopy controls, adjusted OR 1.14, 95 % CI 0.75–1.74). Additionally, exclusion of EGD patients aged < 50 years did not change the results.

Table 3 shows the associations between alcohol consumption and risk of BE. Colonoscopy controls were more likely to be current drinkers (57 %) than endoscopy controls (50 %) and BE cases (54 %). Overall, 91 % of study participants were ex-drinkers or current drinkers and among those 76, 19 and 54 % reported drinking beer, wine and liquor, respectively. We found no statistically significant association between alcohol drinking status and BE. After adjusting for confounding, average consumption of 14 to <28 drinks per week of total alcohol was associated with lower risk of BE (BE vs. colonoscopy controls, OR 0.39, 95 % CI 0.15–1.00). When we analyzed beverage-specific alcohol consumption, the apparent lower risk among those consuming 14 to <28 drinks/week compared to life-long non-drinkers was observed only for beer intake (BE vs. colonoscopy controls, OR 0.50, 95 % CI 0.19–1.35), but was not statistically significant. There was no significant association between alcohol consumption and BE when cases were compared with endoscopy controls.

We found no evidence for effect modification when we stratified the analyses for smoking and alcohol variables by age, WHR, duration of GERD symptoms, *H. pylori* status and presence of hiatal hernia (Supplementary Tables 1 and 2).

Discussion

In this case–control study, we found no evidence that smoking or higher alcohol consumption increased the risk of BE. In contrast, the risk of BE among alcohol drinkers tended to be lower (albeit not statistically significant) than that among life-long non-drinkers. When we examined beverage-specific intake, the apparent inverse association was limited to beer. The null findings were consistent across different strata of known or suspected risk factors for BE.

Cancer studies have provided strong evidence that smoking has a modest adverse effect on the risk of EAC. In a pooled analysis of 12 studies in the BEACON consortium, compared with never smokers, the risk of developing EAC for persons with a heavy smoking history was almost threefold higher (≥45 pack-years of smoking exposure, OR 2.71, 95 % CI 2.16–3.40) [12]. However, whether smoking acts early in the metaplasia-dysplasia-carcinoma sequence in the esophagus by initiating the development of BE or later by promoting the development of EAC in patients with BE cannot be determined from these cancer studies.

Four recent well-conducted case–control studies have previously examined the association between smoking and risk of developing BE, with conflicting results. In their Australian study, Smith et al. [14] found a statistically significant association between smoking status and BE. Compared to never smokers, former and current smokers had twofold higher risk of BE, but risk did not increase with pack-years of exposure (p-trend = 0.32) [14]. With results similar to the current study, there was no association between smoking and BE in the all-Ireland FINBAR study [16]. While the FINBAR study showed a strong association between smoking and EAC (~fivefold higher risk for current smokers), even being a heavy smoker did not infer greater risk of BE (>40 pack-years compared to never smokers, OR 1.28, 95 % CI 0.76–2.17). Likewise, a case–control study conducted in Northern California also found no overall association between smoking and BE (current smokers, OR 1.09, 95 % CI 0.68–1.74) [17]. Finally, in a study conducted in western Washington State, Edelstein et al. [15] found higher risk among ever smokers (OR 2.1, 95 % CI 1.4–3.1). However, similar to the current study, there was no increased risk of BE among current smokers (OR 1.4, 95 % CI 0.8–2.5). A pooled analysis of these four studies found a statistically significant increased risk of BE among persons with 45 or more pack-years of smoking (OR 1.92, 95 % CI 1.05–3.51), but significant high levels of between-study heterogeneity were present (I^2 = 70 %) [13].

If smoking is associated with BE, what might explain the conflicting results among these studies? It is considered easier to find a significant association, if one exists, among a lower risk population with low population-level exposure to the risk factor. In the current study as well as the FIN-BAR and Northern Californian studies [16, 17], the rates of ever smoking and heavy smoking (>30 pack-years) were far higher than the corresponding rates in the two studies that found a significant association between smoking and BE [14, 15]. It is possible then that this may explain the lack of association in our study. However, arguing against this explanation, while the FINBAR study found no association with BE, they found a very strong and statistically significant association between smoking and EAC [16]. A plausible explanation relates to the selection of controls in the studies. Some BE studies, including ours, are based on direct evaluation of the esophagus by endoscopy in controls. In contrast, others used population-derived controls that have not generally undergone endoscopy. It is possible that controls in studies like ours are more likely to have risk factors (e.g., smoking) for gastrointestinal disease or symptoms than controls in studies where endoscopy was not used to define controls. While this may attenuate the association between smoking and BE in endoscopy-based studies, it does not explain the lack of association reported in some population-based studies.

Notably, a developing body of evidence indicates that smoking may instead promote the progression of BE to EAC. In three studies to date, smoking has been associated with approximately twofold higher risk of EAC in patients with BE [18–20]. The validity of this relationship is supported by evidence for a dose–response relationship. In their large cohort study, Hardikar et al. [18] found that EAC risk increased linearly with increasing pack-years of smoking among BE patients who smoked (p-trend = 0.02). The exact mechanisms are unknown however. As smoking is known to cause DNA damage on Barrett's mucosa, it is posited that the resulting DNA damage may promote cell division and proliferation of

malignant columnar epithelial cells and lead to cancer progression [28]. Smoking may preferentially increase the likelihood of developing “high-risk” BE, such as long segment BE, which is more likely to progress to EAC. Therefore, the risk of BE in smokers would be less elevated than the observed risk for cancer. However, we compared the effects of smoking on the likelihood of developing long versus short segment BE and found no differences.

This study adds to evidence from previous investigations that show no association between higher alcohol intake and increased risk of developing EAC and BE [21–25], and no association with risk of progressing from BE to EAC [18]. In contrast, with results similar to the current study, moderate to high intake of beer has been associated with lower risk of EAC (≥5 drinks/day, OR 0.63, 95 % CI 0.40–0.99) and BE (≥3 drinks/day, OR 0.49, 95 % CI 0.25–0.96) in previous studies [21, 25]. While alcohol is therefore not a key factor in the prevention of EAC, alcohol is associated with increased risks of esophageal squamous cell carcinoma and other cancers [29, 30] and the importance of this inverse association is limited.

The strengths of this study include the large sample size, well-defined groups of cases and controls, the collection of information on a wide range of potential confounders and the systematic collection of detailed smoking and alcohol data. We used comprehensive measures of lifetime exposure to smoking and alcohol to ensure that changes in use were captured and integrated into measures of overall exposure. The lack of associations with smoking and alcohol are unlikely to be explained by differential reporting as we ascertained questionnaire data prior to the study EGD (before case and control status was defined) to minimize the possibility of biased recall. Finally, we used standardized endoscopic and histologic criteria throughout the study ascertainment period and included only BE patients with histopathologically diagnosed BE to avoid misclassification.

This study has a few limitations. The overall response rate among the primary care group was 43 % and this may have biased our results. However, participants who consent are generally healthier than the general population and, if one existed, this would strengthen an association. A limitation of this study is that we had small numbers of wine drinkers and we were unable to examine the effects of high wine intake. Likewise, BE case numbers were small in some strata of the stratified analyses. Lastly, as most participants in the VA study were White men and the characteristics of VA and non-VA populations may differ, our findings may not be generalizable to women or non-White men from the general non-VA population.

In summary, we found no evidence that smoking or higher alcohol consumption were associated with increased risk of developing BE. Smoking increases the risk of developing EAC, albeit through promoting progression of BE to EAC rather than initiating BE in the first place.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Characteristics of controls and cases

Variable	BE cases *n* = 258 *n* (%)	Colonoscopy controls *n* = 453 *n* (%)	BE cases versus colonoscopy controls *p* value[a]	Endoscopy controls *n* = 1,145 *n* (%)	BE cases versus endoscopy controls *p* value[a]
Age, mean (SD)	61.7 (7.6)	62.2 (6.7)	0.39	60.1 (8.6)	0.01
Sex, males	252 (97.7)	437 (96.5)	0.37	1,015 (88.7)	<0.001
Race					
White	227 (88.0)	248 (54.7)	<0.001	724 (63.2)	<0.001
African American	28 (10.8)	196 (43.3)		382 (33.4)	
Other	3 (1.2)	9 (2.0)		39 (3.4)	
GERD duration					
No GERD	94 (36.4)	336 (74.2)	<0.001	517 (45.2)	0.01
1 to <15 years	22 (8.5)	19 (4.2)		121 (10.6)	
15 to <30 years	59 (22.9)	43 (9.5)		201 (17.5)	
≥30 years	62 (24.0)	378 (8.4)		215 (18.8)	
Missing information	21 (8.1)	17 (3.7)		91 (7.9)	
PPI use	188 (72.9)	99 (21.9)	<0.001	718 (62.7)	0.002
NSAID intake	157 (60.9)	284 (62.7)	0.63	650 (56.8)	0.23
Body mass index					
Normal	40 (15.5)	71 (15.7)	0.95	236 (20.6)	0.10
Overweight	93 (36.1)	158 (34.9)		424 (37.0)	
Obese	125 (48.4)	224 (49.4)		485 (42.4)	
WHR					
Low WHR	20 (7.7)	62 (13.7)	0.01	179 (15.6)	0.001
High WHR	237 (91.9)	384 (84.8)		931 (81.3)	
Missing information	1 (0.4)	7 (1.5)		35 (3.1)	
H. pylori status					
Negative	202 (78.3)	283 (62.5)	<0.001	767 (67.0)	<0.001
Positive	43 (16.7)	162 (35.8)		317 (27.7)	
Missing information	13 (5.0)	8 (1.8)		61 (5.3)	

BE Barrett's esophagus, *GERD* gastroesophageal reflux disease, *NSAID* non-steroidal anti-inflammatory drug, *PPI* proton pump inhibitor, *SD* standard deviation, *WHR* waist-to-hip ratio

[a]Participants with missing information were excluded from the student's *t* test or Chi square test, where appropriate

Table 2

Unadjusted and adjusted odds ratios for associations between smoking-related variables and risk of Barrett's esophagus

	BE	Colonoscopy controls			Endoscopy controls		
	n	*n*	Unadjusted OR (95 % CI)	Adjusted OR[a] (95 % CI)	*n*	Unadjusted OR (95 % CI)	Adjusted OR[a] (95 % CI)
Smoking status							
Never smoker[b]	60	113	1.00 (ref)	1.00 (ref)	318	1.00 (ref)	1.00 (ref)
Ever smoker	198	340	1.10 (0.77–1.57)	0.84 (0.53–1.32)	827	1.27 (0.93–1.74)	1.09 (0.78–1.52)
Ex-smoker	110	205	1.01 (0.69–1.49)	0.74 (0.45–1.22)	438	1.33 (0.94–1.88)	1.06 (0.73–1.53)
Current smoker	88	135	1.23 (0.81–1.85)	0.99 (0.59–1.68)	389	1.20 (0.84–1.72)	1.12 (0.77–1.64)
Smoking intensity (cigarettes/day)							
≤15	61	158	0.73 (0.47–1.12)	0.64 (0.38–1.11)	307	1.05 (0.71–1.55)	1.17 (0.77–1.76)
15.01–20	65	101	1.21 (0.78–1.89)	1.04 (0.60–1.81)	276	1.25 (0.85–1.84)	1.02 (0.68–1.52)
> 20	71	81	1.65 (1.06–2.58)	0.91 (0.52–1.59)	243	1.55 (1.06–2.27)	1.08 (0.72–1.62)
p-trend[c]			< 0.001	0.27		0.05	0.80
Age at smoking initiation (years)							
≤15	67	104	1.21 (0.78–1.88)	0.76 (0.44–1.32)	275	1.29 (0.88–1.90)	1.03 (0.69–1.54)
16–18	81	125	1.22 (0.80–1.86)	1.01 (0.60–1.71)	308	1.39 (0.96–2.02)	1.14 (0.78–1.68)
> 18	49	111	0.83 (0.53–1.32)	0.71 (0.40–1.27)	244	1.06 (0.70–1.61)	1.07 (0.69–1.65)
p-trend[c]			0.11	0.85		0.39	0.75
Smoking duration (years)							
≤25	70	121	1.09 (0.71–1.67)	0.79 (0.46–1.36)	255	1.46 (0.99–2.13)	1.21 (0.81–1.81)
25.01–40	67	134	0.94 (0.61–1.45)	0.72 (0.41–1.26)	320	1.11 (0.76–1.63)	1.04 (0.70–1.56)
> 40	61	85	1.35 (0.86–2.13)	1.05 (0.60–1.84)	252	1.28 (0.87–1.90)	1.01 (0.66–1.53)
p-trend[c]			0.52	0.49		0.40	0.43
Pack-years of smoking							
≤15	50	122	0.77 (0.49–1.22)	0.66 (0.37–1.17)	240	1.10 (0.73–1.67)	1.05 (0.68–1.61)
15.01–40	74	130	1.07 (0.70–1.64)	0.94 (0.55–1.60)	320	1.23 (0.84–1.78)	1.16 (0.79–1.72)
> 40	73	88	1.56 (1.01–2.43)	0.91 (0.53–1.59)	266	1.46 (1.00–2.12)	1.03 (0.69–1.54)
p-trend[c]			0.002	0.34		0.17	0.96
Smoking cessation (years)							

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	BE	Colonoscopy controls			Endoscopy controls		
	n	*n*	Unadjusted OR (95 % CI)	Adjusted OR[a] (95 % CI)	*n*	Unadjusted OR (95 % CI)	Adjusted OR[a] (95 % CI)
≤15	42	76	1.04 (0.64–1.70)	0.73 (0.39–1.37)	176	1.27 (0.82–1.95)	1.12 (0.71–1.77)
15.01–30	37	70	1.00 (0.60–1.65)	0.86 (0.46–1.62)	171	1.15 (0.73–1.80)	0.86 (0.53–1.39)
> 30	31	59	0.99 (0.58–1.69)	0.57 (0.29–1.13)	91	1.81 (1.10–2.95)	1.23 (0.72–2.09)
p-trend[c]			0.86	0.56		0.25	0.66

BE Barrett's esophagus, *CI* confidence interval, *OR* odds ratio

[a] Adjusted for age, sex, race, duration of GERD symptoms, WHR, *H. pylori* infection, PPI use and NSAID use

[b] Reference group for all analyses is never smokers

[c] *p* for trend excludes never smokers

Table 3

Unadjusted and adjusted odds ratios for associations between alcohol-related variables and risk of Barrett's esophagus

	BE	Colonoscopy controls			Endoscopy controls		
	n	*n*	Unadjusted OR (95 % CI)	Adjusted OR[a] (95 % CI)	*n*	Unadjusted OR (95 % CI)	Adjusted OR[a] (95 % CI)
Drinking status							
Non-drinker[b]	21	28	1.00 (ref)	1.00 (Ref)	113	1.00 (Ref)	1.00 (Ref)
Ex-drinker	97	165	0.78 (0.42–1.46)	0.71 (0.32–1.56)	458	1.14 (0.68–1.91)	0.98 (0.57–1.69)
Current drinker	140	260	0.72 (0.39–1.31)	0.57 (0.26–1.23)	574	1.31 (0.80–2.17)	1.19 (0.70–2.03)
Average lifetime total alcohol consumption (drinks/week)							
< 7	63	138	0.61 (0.32–1.15)	0.49 (0.21–1.11)	294	1.15 (0.67–1.98)	1.01 (0.57–1.78)
7 to < 14	38	60	0.84 (0.42–1.70)	0.84 (0.34–2.09)	152	1.35 (0.75–2.42)	1.27 (0.68—2.36)
14 to < 28	26	65	0.53 (0.26–1.10)	0.39 (0.15–1.00)	148	0.95 (0.51–1.77)	0.84 (0.44–1.63)
≥28	79	106	0.99 (0.53–1.88)	0.81 (0.35–1.90)	298	1.43 (0.84–2.42)	1.11 (0.63–1.95)
p-trend[c]			0.03	0.13		0.27	0.74
Average lifetime beer consumption (drinks/week)							
< 7	65	160	0.54 (0.29–1.02)	0.53 (0.23–1.19)	333	1.05 (0.61–1.80)	0.94 (0.53–1.66)
7 to < 14	27	45	0.80 (0.38–1.68)	0.72 (0.28–1.88)	101	1.44 (0.77–2.70)	1.29 (0.66–2.51)
14 to < 28	22	44	0.67 (0.31–1.43)	0.50 (0.19–1.35)	118	1.00 (0.52–1.92)	0.87 (0.44–1.73)
≥28	66	86	1.02 (0.53–1.96)	0.76 (0.32–1.80)	215	1.65 (0.96–2.84)	1.27 (0.71–2.27)
p-trend[c]			0.01	0.29		0.03	0.17
Average lifetime wine consumption (drinks/week)							
< 7	25	47	0.71 (0.34–1.49)	0.71 (0.24–2.13)	137	0.98 (0.52–1.85)	1.09 (0.55–2.17)
≥7	13	19	0.91 (0.37–2.25)	1.08 (0.28–4.14)	74	0.95 (0.45–2.00)	1.04 (0.46–2.33)
p-trend[c]			0.56	0.67		0.92	0.68
Average lifetime liquor consumption (drinks/week)							
< 7	63	111	0.76 (0.40–1.44)	0.63 (0.27–1.51)	291	1.17 (0.68–2.00)	1.08 (0.61–1.93)
7 to < 21	32	49	0.87 (0.42–1.79)	1.10 (0.41–2.92)	140	1.23 (0.67–2.25)	1.19 (0.62–2.27)
≥21	36	46	1.04 (0.51–2.13)	0.93 (0.34–2.51)	141	1.37 (0.76–2.48)	1.12 (0.60–2.10)
p-trend[c]			0.25	0.47		0.48	0.93

BE Barrett's esophagus, *CI* confidence interval, *OR* odds ratio

[a] Adjusted for age, sex, race, duration of GERD symptoms, WHR, *H. pylori* infection, PPI use and NSAID use

[b] Reference group for all analyses is life-long non-drinkers

[c] *p* for trend excludes life-long non-drinkers