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Cigarette Smoking and the Risk of Barrett's Esophagus

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Abstract

Introduction—We examined the association between smoking and the risk of Barrett's esophagus (BE), a metaplastic precursor to esophageal adenocarcinoma.

Methods—We conducted a case-control study within the Kaiser Permanente Northern California population. Patients with a new diagnosis of BE (n=320) were matched to persons with gastroesophageal reflux disease (GERD) (n=316) and to population controls (n=317). Information was collected using validated questionnaires from direct in-person interviews and electronic databases. Analyses used multivariate unconditional logistic regression that controlled for age, gender, race and education.

Results—Ever smoking status, smoking intensity (pack-years), and smoking cessation were not associated with the risk of BE. Stratified analyses suggested that ever smoking may be associated with an increased risk of BE among some groups (compared to population controls): persons with long-segment Barrett's esophagus (odds ratio [OR]=1.72, 95% confidence interval [CI] 1.12-2.63); subjects without GERD symptoms (OR=3.98, 95% CI 1.58-10.0); obese subjects (OR=3.38, 95%CI 1.46-7.82); and persons with a large abdominal circumference (OR=3.02, 95%CI (1.18-2.75)).

Conclusion—Smoking was not a strong or consistent risk factor for BE in a large community-based study, although associations may be present in some population subgroups.

Keywords

Smoking; Barrett's esophagus; Gastroesophageal reflux disease; esophageal adenocarcinoma

Background

The incidence of esophageal adenocarcinoma is rising more rapidly than that of any other malignancy in many countries, but relatively little is known about the carcinogenic sequence leading to cancer development.[1-3] Barrett's esophagus, a metaplastic transformation of the esophageal squamous epithelium into specialized intestinal columnar epithelium, is a potentially preneoplastic change in the esophageal lining;[4] persons with Barrett's esophagus have a 30-125-fold increased risk of developing esophageal adenocarcinoma compared to the general population.[5] While cigarette smoking is of substantial importance in the causation of esophageal squamous cell carcinoma,[1,6] its associations with esophageal adenocarcinoma and Barrett's esophagus are less well defined.

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Though there have been no cohort study to our knowledge examining the association between smoking and esophageal adenocarcinoma or Barrett's esophagus, several case-control studies have suggested that smoking increases the risk of esophageal adenocarcinoma,[7-15] and that this increased risk may persist for many years after smoking cessation.[9,16] Cancer studies, however, cannot evaluate whether smoking affects the early stage of carcinogenic pathway. Evaluation of risk factors for Barrett's esophagus may provide information on early events in the carcinogenic pathway for esophageal adenocarcinoma and is of considerable clinical interest, since the treatment or prevention of Barrett's esophagus presents the potential for early risk modification.[17] Some small studies have also suggested that smoking was not clearly associated with the progression from Barrett's esophagus to esophageal adenocarcinoma.[18, 19] In addition, the sustained increase in risk of cancer after smoking cessation raises the possibility that it may, instead, increase the risk of Barrett's esophagus itself.

Some case-control studies have reported an adverse association between cigarette smoking and the risk of Barrett's esophagus,[20,21] while others found no association.[7,22] Differences in the case and comparison groups may explain some of the differences seen in these studies. Most studies included persons with long-standing diagnoses of Barrett's esophagus; the diagnosis of a disease such as Barrett's esophagus may influence behavior patterns. The use of population controls may also not provide sufficient numbers of GERD patients to estimate the effect of a risk factor independent of GERD symptoms (which is a strong risk factor for Barrett's esophagus). Finally, most of these studies did not provide detailed analyses of whether smoking compounded the risk of other risk factors such as abdominal obesity or alcohol. A recent Australian study, which evaluated the interaction between GERD symptoms and smoking, suggested that smokers with frequent GERD were at a significantly higher risk of Barrett's esophagus, compared to non-smokers with GERD.[23] However, these estimates had extremely wide confidence intervals due to the small number of controls with GERD, making definitive interpretations difficult.

Thus, to evaluate the association between smoking and Barrett's esophagus in general population, we conducted a community-based case-control study using persons with a new diagnosis of Barrett's esophagus (cases) and two comparison groups: population controls and GERD controls. The population controls provide an overall evaluation of the association between smoking and the risk of Barrett's esophagus. The GERD controls permit an evaluation of whether smoking is a risk factor among persons with GERD and a more well-powered evaluation of whether any overall association may be mediated by GERD.

Methods

Study Population

The details of the study design have been described previously.[24] Briefly, this was a case-control study conducted within the Kaiser Permanente, Northern California (NCKP) population, an integrated health services delivery organization. NCKP contains approximately 3.3 million persons; the membership has demographics that closely approximate the underlying census population of Northern California.[25,26] Potentially eligible subjects were all adult (ages 18-79 years) NCKP members who were continuously enrolled for at least 2 years prior to their index period, met the case or control definitions outlined below, and were able to understand spoken and written English. The index date for cases was the date of Barrett's esophagus diagnosis. The index date for controls was the midpoint of each 2-3 month selection interval for the cases. The questionnaires asked participants to report exposures in the year prior to their index date. The population and GERD comparison groups were frequency matched to the cases by gender (given the high proportion of males among Barrett's esophagus patients), age at the index date, and geographic region (each subject's home facility).

Case Definition

Cases were eligible NCKP members with a new diagnosis of Barrett's esophagus between October, 2002 and September, 2005, using the International Classification of Disease, 9th revision (ICD-9) code 530.2 (which at NCKP is uniquely coded as "Barrett's esophagitis"), or the College of American Pathologists code 73330 ("Barrett's esophagus"). A single board-certified gastroenterologist (DAC) then reviewed the endoscopy and pathology records of potentially eligible cases. Subjects were included if the endoscopist clearly described a visible length of columnar-type epithelium proximal to the gastroesophageal junction/gastric folds, this area was biopsied, and the biopsies showed specialized intestinal epithelium.[17] The following patients were excluded: patients with only gastric-type metaplasia of the esophagus on all pathologic evaluations; patients with columnar metaplasia without features of intestinal metaplasia on all pathology readings; patients without a biopsy of esophageal origin; biopsies of only a mildly irregular squamocolumnar junction (i.e. an "irregular z-line"); and patients with a prior Barrett's esophagus diagnosis. Pathology slides underwent a separate manual review by a gastrointestinal pathologist (GJR).

Population Controls

Population controls were randomly selected from among all members who lacked an electronic diagnosis of Barrett's esophagus at the time the Barrett's esophagus cases were identified.

GERD Comparison Group

GERD comparison group members were randomly selected from persons with the following characteristics prior to their index date: a GERD-related diagnosis code (ICD-9 codes 530.11 [reflux esophagitis) or 530.81 [gastroesophageal reflux]); a prescription for at least 90 days supply of a histamine-2 receptor antagonist or a proton pump inhibitor (medications used for treating GERD symptoms) in the previous year (from electronic pharmacy records); no prior diagnosis of Barrett's esophagus; and an esophagogastroduodenoscopy close to the index date that did not demonstrate esophageal columnar metaplasia of any type.

Exposure Measurements

During the interview, a structured questionnaire was administered by trained interviewers, and information was collected on GERD symptoms, medication use, medical history, and tobacco use. Anthropometric measurements and blood samples were also taken during the interview. Additional demographic information, medical history, and medication use were collected from electronic databases.

Questionnaire smoking data included the intensity of its use and the ages smoking started and stopped. A current smoker was someone who smoked cigarettes during the month prior to the interview date. A nonsmoker was someone who smoked less than 20 packs over their lifetime. More limited data were also available on pipe, chewing tobacco, and cigar use.

Statistical Analysis

The study utilized standard analytic techniques for evaluating frequency-matched case-control studies, including unconditional logistic regression to calculate odds ratios (ORs) as an estimate of the relative risk.[27-29] We first compared Barrett's esophagus cases vs. population controls to examine the association between smoking and Barrett's esophagus in general population, and to evaluate the effect of smoking among individuals with GERD, cases were compared to GERD controls. The following additional variables were evaluated as potential confounders: race/ethnicity (classified as Caucasian vs. non-Caucasian due to small sample sizes in the ethnic subgroups), education, body mass index (BMI=kg/m^2), aspirin or nonsteroidal anti-inflammatory drug (NSAID) use, total energy intake (kcal/day), alcohol use (number of drinks/

day), Helicobacter pylori infection status (H.pylori), and a comorbidity index (the DxCg score, which creates a predictive comorbidity score based on demographic data, medical coding, and pharmacy utilization). Confounders were included in the final model if their inclusion altered the β coefficient by >10%.

First, we analyzed the risk of Barrett's esophagus by cigarette smoking status: current smokers, recent quitters (those who have quit less than 10 years ago), ever smokers, and non-smokers. Second, we analyzed the effects of smoking intensity (average number of packs/day times the number of years smoking), and smoking cessation (amount of time since the subject quit smoking). Third, we examined whether the effects of smoking were modified by other risk factors by stratifying the results by GERD symptoms (more than once a week vs. never/less than once a month), alcohol use (none vs. at least one serving per day), obesity (BMI>30 vs. BMI 18.5-25), and abdominal obesity (1^{st} quartile vs. 3^{rd}&4^{th} quartiles of abdominal circumference). The estimated risk for each subgroup was compared to the absolute reference category (i.e., non-smokers who have no GERD, non-drinker, normal BMI, or 1^{st} quartile abdominal circumference, respectively) in separate multivariate analyses for each strata (controlling for age and gender). For abdominal obesity analyses, the model was also adjusted for BMI. Finally, we evaluated whether the main effects differed by the length of the Barrett's esophagus segment (<3 centimeters vs. ≥3 centimeters).

We evaluated for the possibility of non-response bias (differences between participants vs. non-participants) by analyzing a brief telephone interview and available electronic data (BMI codes, smoking status, ethnicity, age, gender, number of health visits, DxCg score) from potentially eligible subjects who could not be contacted or who declined participation.

All studies were analyzed using STATA statistical software (version 8, STATA Corporation, College Station, TX) and all tests of statistical significance are two sided. The study and analyses were approved by the institutional review board.

Results

Baseline characteristics

The demographic characteristics were fairly evenly distributed among the three groups, although cases had a slightly higher proportion of ever smokers compared to the other groups (Table 1). Among the cases, the length of the Barrett's segment was <3 centimeters in 118 subjects (37%), ≥3 centimeters in 151 subjects (47%), and the length was not reported in 51 subjects (16%).

Overall smoking status

Neither “ever smoker” nor “current smoker” was significantly associated with the overall risk of Barrett's esophagus when cases were compared to population controls (Table 2). For instance, current smokers were not at significantly increased risk compared to non-smokers [OR=1.09 95% CI (0.68-1.74)].

Smoking intensity and time since smoking cessation

Subjects who quit smoking more recently (within 15 years prior to the index date) were at a higher risk of developing Barrett's esophagus than nonsmokers, though the results were of borderline significance (Table 2). There was no statistically significant association between smoking intensity (number of pack-years smoked) and the risk of Barrett's esophagus(Table 3).

Interactions between smoking, obesity, alcohol and GERD

There was no statistical evidence for synergistic/multiplicative interaction between smoking and other risk factors in the logistic regression models (p values >0.1 for all comparisons below); however, potential non-multiplicative interactions were seen between ever smoking and certain other risk factors, as described below. All discussions below compare cases vs. the population controls (Table 4), unless otherwise noted.

GERD symptoms—Smoking increased the risk of Barrett's esophagus among persons without GERD symptoms [OR=3.98, 95% CI (1.58-10.0)]. GERD symptoms were a strong independent risk factor for Barrett's esophagus, but the addition of smoking did not markedly increase the risk of Barrett's esophagus beyond that seen with GERD alone (Table 4).

Alcohol—Smokers who drank at least one drink of alcohol per day had approximately a two-fold increased risk of Barrett's esophagus, although these associations were of borderline significance and the confidence intervals included 1.0.(Table 4). On the other hand, alcohol users who did not smoke were at lower risk of having Barrett's esophagus, though the confidence interval included 1.

Body Mass Index—Obese subjects (BMI≥30) who smoked had an increased risk of Barrett's esophagus [(OR=3.38, 95% CI (1.46-7.82)] compared to non-smokers with normal BMI (Table 4). In contrast, being obese was not an independent risk factor of Barrett's esophagus among non-smokers (OR=1.35 95%CI(0.69-2.67)).

Abdominal Obesity—Persons with abdominal obesity (3^{rd} or 4^{th} quartile) who smoked had a three-fold increase in the risk of Barrett's esophagus compared to non-smokers in the first quartile of abdominal circumference, adjusting for body mass index (OR=3.02 95% CI (1.18-2.75)), though most of this increase in risk appeared to come from the increased abdominal size alone. There was no substantial increase in risk between smokers with abdominal obesity vs. nonsmokers with abdominal obesity.

Effect of smoking among subjects with GERD

We evaluated whether smoking was a risk factor for Barrett's esophagus among individuals with GERD by comparing cases to GERD controls who lacked Barrett's esophagus on endoscopy (Table 5). These analyses effectively helped “match” for a GERD-type diagnosis and for health-care seeking behaviors leading to an endoscopy. For this comparison, the patterns of the associations were similar to case vs. population control comparison, though they were weaker and not statistically significant. For instance, the strongest association was found among recent quitters (5-14.9 years before index date) [OR=3.42 95%CI(1.24-9.43)].

When stratified, alcohol users who smoked had an increased risk of Barrett's esophagus [OR=3.74 95%CI(1.63-8.56)] compared to subjects who neither drank nor smoked. On the other hand, the odds ratios for interactions with BMI and abdominal obesity were not statistically significant (data not shown).

Supplemental Analyses

Lengths of Barrett's segment—Ever-smoking was adversely associated with the risk of long segment Barrett's esophagus (>3cm) [OR=1.72, 95% CI (1.12-2.63)] after adjusting for age, gender, race, and education, while there was no association with short segment Barrett's esophagus [OR=1.19, 95%CI (0.76-1.85)]. There was no association between segment length and smoking intensity or time since smoking cessation (data not shown).

Cigar, pipe, chewing tobacco—There was no association between ever smoking cigar, pipe, or chewing tobacco and the risk of Barrett's esophagus. When cases were compared to population controls, the risks did not differ substantially from never users [OR=1.02 95%CI (0.66-1.57); OR=0.83 95%CI(0.54-1.27); OR=0.74 95%CI(0.36-1.51), respectively.]

Analyses for confounding and bias—The evaluation of additional potential confounders did not demonstrate any evidence of confounding by body mass index (BMI=kg/m^2), recent alcohol use (number of drinks/week), aspirin or nonsteroidal anti-inflammatory drug (NSAID) use, total caloric intake, a comorbidity index (the DxCg score), H. pylori status, or geographic location of the subject. A fully adjusted model for ever smoking (containing all these factors plus age, gender, race, and education) (OR=1.40, 95% CI 0.94-1.91), cases vs. population controls) was similar to a model that contained only age, gender, race, and education [(OR=1.32, 95%CI 0.94-1.85).] For smoking cessation analyses, the model was also adjusted pack-years of smoking.

Discussion

We found no strong or consistent overall association between smoking and the risk of Barrett's esophagus in a large, community-based case-control study. Those who have quit smoking less than 15 years prior to the index date were at ahigher risk of having Barrett's esophagus, though this may be explained by individuals who develop symptoms a few years prior to diagnosis and quit smoking, resulting also in the lower observed risk among current smokers than more recent quitters. Our stratified analyses suggested smoking may increase the risk of Barrett's esophagus among some groups, such as persons who are obese, have a large abdominal circumference, or who drink at least one alcoholic beverage per day. Smoking did not markedly increase the risk of BE among persons with a diagnosis of GERD.

This study complements previous analyses that reported adverse effects of smoking on the risk of esophageal adenocarcinoma;[7-16] however, those studies could not evaluate whether smoking act on the early stage in the carcinogenic pathway. The current study evaluated a specific potential step in the carcinogenesis process by evaluating the risk of Barrett's esophagus. Two other recent population-based studies found inconsistent results between smoking and Barrett's esophagus. A study from Ireland found no association when comparing heavy smokers (>40 pack years) vs. non-smokers (OR=1.28, 95% CI 0.76-2.17).[7] A study from the state of Washington found an association between ever smoking and Barrett's esophagus, but, similar to the current study, found no association for current smokers (OR=1.0, 95% CI 0.5-2.2), no association with smoking intensity, and a greater risk for former smokers than for current smokers, making inferences for clear causation more difficult.[20]

An important question is whether smoking may increase the risk of Barrett's esophagus among persons with GERD. An Australian study by Smith et al. suggested a strong synergistic effect between the two factors (OR=51.4, 95% CI (14.1-188) for GERD patients who smoked vs. OR=16.9, 95% CI (4.2-68) for GERD patients who did not smoke, both comparing to non-smokers without GERD), although the confidence intervals were wide due to small sample size in each category.[23] In contrast, the current study found, using a GERD comparison group of 316 subjects, that smoking did not increase the risk of Barrett's esophagus among persons with a GERD diagnosis. Similarly, analyses of the cases vs. the population controls, stratified by GERD symptoms, also did not suggest a synergistic association between smoking and GERD. The authors of the Australian study cautiously concluded that smoking is “neither a necessary nor sufficient” factor for Barrett's esophagus,[23] and the confidence intervals for the risk of smoking among those without reflux symptoms (OR=2.4, 95% CI 0.9-6.8), although not statistically significant, overlapped our results. It should be noted, however, that both our

study and the Australian study had wide confidence intervals for these effect estimates, making it difficult to determine whether there is a synergistic effect between GERD and smoking.

The current study did suggest possible non-multiplicative interactions between smoking and alcohol use and between smoking and measures of obesity (BMI and abdominal circumference). Although drinkers who do not smoke and persons with a normal BMI may have other "health-conscious behaviors", adjustments for diet and income did not substantially change the main associations found (data not shown), though adjustment for education attenuated the results slightly. The influence of smoking on the obesity-Barrett's esophagus relationship may be partially mediated by GERD symptoms: obesity may increase GERD,[30] and smoking or nicotine intake may also cause GERD by reducing lower esophageal sphincter pressure,[31,32] reducing the acid clearance from the esophagus,[33,34] or increasing gastric acid secretion.[35] When the data for the joint effect (smokers *and* obese) were adjusted for the presence of GERD symptoms (once a week or more of at least moderate severity), the smoking-Barrett's esophagus association was reduced substantially (from OR=3.38 to OR=1.19, cases vs. population controls). The potential mechanistic interactions between smoking, GERD, obesity and Barrett's esophagus are complex, but some of the smoking-Barrett's esophagus association among the obese may be mediated by GERD (either from smoking or from obesity). This association may also explain why the results were weaker when GERD patients were used as the comparison group.

It is unclear why there was a difference between subjects with longer vs. shorter segments of Barrett's esophagus: the study utilized rigorous criteria which excluded persons with only minimal changes at the gastroesophageal junction ("irregular z-lines"), and prior studies of this population looking at obesity and helicobacter pylori did not find substantial differences in risk between the cases with longer vs. shorter segments.

There are several strengths of this study. First, the study was large; it contained approximately three times as many cases with endoscopically documented Barrett's esophagus as the only other United States study and it analyzed a large group of GERD controls. This size increases the power and precision of the estimates.[20] Second, subjects came from a diverse population base that closely approximates the region's census demographics; thus, the results can likely be generalized to similar large populations. Third, the study used only new diagnoses of Barrett's esophagus and we identified all subjects with a new diagnosis within the population. The use of prevalent cases or referral cases may select for patients with a different clinical course or patients compliant with follow-up; prevalent cases may also have initiated changes in smoking habits or other behaviors after their Barrett's esophagus diagnosis.[36] The use of new diagnoses thus minimizes selection bias and provides the most valid evaluation of the entire population of Barrett's esophagus patients and may partially explain differences between the results of this study and studies that included subjects with long-standing diagnoses of Barrett's esophagus. Third, the availability of a GERD comparison group provided information on the risk of Barrett's esophagus among patients with GERD.

There are potential limitations of this study. First, case-control studies cannot definitively establish cause and effect.[29] Observational studies are subject to confounding by other unmeasured variables; although analyses that evaluated several potential confounders provided little evidence of confounding, we cannot exclude the possibility that some measured or unmeasured factors might have influenced the results. Second, although the study was powered to look at overall associations, the power to detect differences in the stratified subgroups was more limited. Although we limited the number of subgroups examined a priori, the evaluation of small subgroups can detect associations present solely due to chance which warrants cautious interpretation of the subgroup analyses. Third, population samples may not represent the underlying population through chance or bias. Our results, of no overall association between

smoking and Barrett's esophagus, could be biased if the smoking rate among our sample of population controls was artificially higher than the “true” average rate among our membership; however, comparisons with other studies provided no evidence for this bias. A recent Kaiser Permanente Northern California stratified random sample health survey of over 18,000 members found that 10.7% of males 45-64 years of age were “current smokers”;[37] this number is almost identical to the 11.1% proportion found among males ages 45-64 in the current study's population control group. A 2004 California Adult Tobacco Survey (conducted by the California Department of Health Services for the entire state), found that 15.1 percent of all persons (both males and females) ages 45-64 were “current smokers” throughout the state.[38] Neither of these studies suggested our population control smoking rate was artificially high. Using electronic data, our participants also did not differ significantly from non-participants by gender, a recorded smoking diagnosis, or BMI diagnoses. Participants were somewhat less likely to be Asian or Hispanic, were slightly older (62 years vs. 59 years), and had a slightly higher total comorbidity score (2.8 vs. 2.0, $p<0.01$), but adjustment for these factors did not influence the results presented.

In summary, smoking was not an overall risk factor for Barrett's esophagus in a large community-based study, although we cannot exclude the possibility of small effects. Smoking also did not increase the risk of Barrett's esophagus among people with GERD. There were modest associations between smoking and Barrett's esophagus in subgroups of persons with obesity, abdominal obesity, and alcohol use, although the small size of these subgroups warrants cautious interpretation of these analyses. These results, combined with existing studies, suggest that although smoking may be a risk factor for esophageal adenocarcinoma, the carcinogenic mechanism may not be through substantially increasing the risk of Barrett's esophagus. Further information is needed to clarify the effect of smoking in higher risk subgroups and its role as a risk factor for the malignant transformation from Barrett's esophagus into esophageal adenocarcinoma.

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Table 1

Characteristics of study groups

	Cases	GERD controls	Population controls
	Number or Mean (% or standard deviation)	**Number or Mean (% or standard deviation)**	**Number or Mean (% or standard deviation)**
Number of subjects	320	316	317
Age (years)			
20-39	9 (3)	12 (4)	9 (3)
40-59	120 (38)	116 (37)	105 (33)
60-79	191 (59)	188 (59)	203 (64)
Race			
White	261 (82)	249 (79)	264 (83)
Hispanic	25 (8)	20 (6)	13 (4)
Black	5 (2)	21 (7)	17 (5)
Asian	19 (6)	11 (3)	12 (4)
Others/Mixed/Unknown	10 (3)	15 (5)	11 (4)
Gender			
Male	234 (73)	218 (69)	214 (68)
Smoking status			
Non smoker	108 (34)	129 (41)	140 (44)
Current smoker	51 (16)	40 (13)	39 (12)
Ever smoker	212 (66)	187 (59)	176 (56)
Alcohol use status			
Non drinker	99 (31)	114 (36)	85 (27)
Light drinker (<7/wk)	155 (48)	133 (42)	158 (50)
Moderate drinker (7-13/wk)	27 (8)	27 (9)	48 (15)
Heavy drinker (14+/wk)	39 (12)	42 (13)	26 (8)
Body mass index (kg/m^2)	29.5 (±0.3)	28.9 (±0.3)	29.5 (±0.3)

Eligible Barrett's esophagus cases were frequency matched to control groups by gender, age (by 5 year age groups) and center of diagnosis.

Table 2

Adjusted odds ratios (ORs) and corresponding 95% confidence intervals for the risk of Barrett's esophagus in relation to cigarette smoking status and smoking cessation (cases vs. population controls)

	# BE/Pop controls	Cases vs. Population controls OR (95%CI)
Smoking status*		
Non-smoker	108/140	1 (ref)
Ever smoker	212/176	1.32 (0.94-1.85)
Current smoker	51/39	1.09 (0.68-1.74)
All former smokers	161/137	1.35 (0.94-1.94)
# Years since smoking cessation**		
Less than 5years	19/8	3.69 (0.90-15.1)
5-14.9	36/25	2.84 (0.99-8.11)
15-24.9	38/33	1.37 (0.59-3.18)
25+	38/71	1.14 (0.66-1.97)
Per year since quit smoking		0.98 (0.95-1.00)
p-value for trend		0.07

* The model was controlled for age, race (white vs. non-white), gender, and education

** The model was controlled for all the above mentioned variables plus pack-year of smoking.

Table 3

Adjusted odds ratios (ORs) and corresponding 95% confidence intervals for the risk of Barrett's esophagus in relation to total pack-year of tobacco use (cases vs. population controls)

# Packyears	# cases/population	Cases vs. Population OR (95%CI)*
Non-smoker	108/140	1 (ref)
<10	52/43	1.47 (0.90-2.39)
10-30	65/59	1.22 (0.77-1.92)
30-50	48/36	1.32 (0.77-2.28)
50+	47/37	1.13 (0.64-1.99)
Per pack-year		1.00 (0.10-1.01)
p-value for trend		0.688

*The model was controlled for age, race (white vs. non-white), gender, and education

Table 4

Effects of smoking on Barrett's esophagus: stratified by GERD symptoms, alcohol use, body mass index (BMI), and abdominal obesity: Cases vs. Population controls comparison

	Non-smoker		Current smoker or Recent quitter (quit less than 10years ago)	
	N (cases/controls)	OR (95% CI)[1]	N (cases/controls)	OR (95% CI) [1]
GERD symptoms[2]				
never or < once a month	10/100	1 (ref)	15/33	3.98 (1.58-10.0)
≥ once a week	92/29	32.3 (14.8-70.4)	73/20	37.4 (16.2-86.3)
Alcohol use[3]				
Non user	38/46	1 (ref)	25/14	2.20 (0.99-4.92)
1+ drink/day	9/21	0.58 (0.23-1.45)	31/19	2.07 (0.94-4.57)
Body mass index[4]				
Normal (BMI=18.5-24.9)	20/35	1 (ref)	22/18	2.03 (0.87-4.73)
Obese (BMI≥30)	45/58	1.35 (0.69-2.67)	33/19	3.38 (1.46-7.82)
Abdominal obesity (abdominal circumference)[5]				
1st quartile	30/47	1 (ref)	18/14	2.05 (0.86-4.86)
3rd-4th quartiles	61/57	2.42 (0.99-5.91)	48/31	3.02 (1.18-2.75)

[1] The model was controlled for age and gender (except for the abdominal obesity analysis, which was also adjusted for BMI)

[2] Subjects who reported GERD symptoms ≥once a month and <once a week were excluded.

[3] Subjects who reported drinking <1drink/day were excluded.

[4] Subjects with BMI<18.5 (underweight) and 25-<30 (overweight) were excluded.

[5] Subjects in the second quartile of abdominal circumference were excluded, and the model was adjusted for BMI as well.

Table 5

Adjusted odds ratios (ORs) and corresponding 95% confidence intervals for the risk of Barrett's esophagus in relation to cigarette smoking status, smoking cessation, and total pack-year of tobacco use (cases vs. GERD comparison)

	# BE/GERD	Cases vs. GERD controls OR (95%CI)
Smoking status*		
Non-smoker	108/129	1 (ref)
Ever smoker	212/187	1.21 (0.87-1.70)
Current smoker	51/40	1.27 (0.80-2.02)
All former smokers	161/147	1.21 (0.85-1.73)
# Years since smoking cessation**		
Less than 5years	19/14	3.79 (0.93-15.4)
5-14.9	36/33	3.42 (1.24-9.43)
15-24.9	38/39	0.87 (0.41-1.87)
25+	38/31	0.97 (0.54-1.74)
Per year since quit smoking		0.99 (0.96-1.01)
p-value for trend		0.24
# Packyears*		
Non-smoker	108/129	1 (ref)
<10	52/48	1.26 (0.79-2.04)
10-30	65/57	1.24 (0.79-1.95)
30-50	48/30	1.68 (0.97-2.92)
50+	47/49	0.95 (0.55-1.62)
Per pack-year		1.00 (0.99-1.00)
p-value for trend		0.813

* The model was controlled for age, race (white vs. non-white), gender, and education

** The model was controlled for all the above mentioned variables plus pack-year of smoking.