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Dietary glycemic index, glycemic load, and lung cancer risk: a case-control study in Los Angeles County

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Conflict of Interest

The authors declare no conflicts of interest.

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Abstract

Background: Although there is some evidence of positive associations between both the glycemic index (GI) and glycemic load (GL) with cancer risk, the relationships with lung cancer risk remain largely unexplored. We evaluated the associations between GI and GL with lung cancer.

Methods: The analyses were performed using data from a population-based case-control study recruited between 1999 and 2004 in Los Angeles County. Dietary factors were collected from 593 incident lung cancer cases and 1026 controls using a modified food frequency questionnaire. GI and GL were estimated using a food composition table. Adjusted odds ratios (ORs) and 95% confidence intervals (CI) were estimated using unconditional logistic regression adjusting for potential confounders.

Results: Dietary GI was positively associated with lung cancer (OR for upper vs. lower tertile = 1.62; 95% CI: 1.17, 2.25). For histologic subtypes, positive associations were observed between GI and adenocarcinoma (OR for upper vs. lower tertile = 1.82; 95% CI: 1.22, 2.70) and small cell carcinoma (OR for upper vs. lower tertile = 2.68; 95% CI: 1.25, 5.74). No clear association between GL and lung cancer was observed.

Conclusion: These findings suggest that high dietary GI was associated with increased lung cancer risk, and the positive associations were observed for both lung adenocarcinoma and small cell lung carcinoma. Replication in an independent dataset is merited for a broader interpretation of our results.

Keywords

lung cancer; glycemic index; glycemic load; risk factor; epidemiology; lung adenocarcinoma; small cell lung carcinoma

INTRODUCTION

Lung cancer is the second most common cancer and the leading cause of cancer death in the United States [1]. Tobacco smoking is an established risk factor for lung cancer; approximately 80% of lung cancer deaths in the US are attributable to smoking tobacco [2]. However, considerable evidence exists that dietary factors may also influence the risk of lung cancer [3–6]. High dietary carbohydrate consumption could contribute to carcinogenesis by altering the insulin-like growth factor-I (IGF-I) pathway, generating oxidative stress, and/or promoting cell proliferation [7–10].

The glycemic index (GI) and glycemic load (GL) were developed to classify carbohydrate foods based on the postprandial blood glucose response. The higher the GI and GL, the greater the elevation in blood glucose level [11]. A number of epidemiologic studies have reported associations between high GI and/or GL diets with a higher risk for cancers, including colorectal [12–14], pancreatic [15], endometrial [16], esophageal [17], laryngeal

cancer[18] and breast [13, 19, 20]. Other studies, however, found null associations with several cancers [21, 22]. For lung cancer risk, few studies have been published with inconsistent results [23–27]. The limited number of studies with conflicting findings highlights the need for additional investigation of GI and GL on lung cancer risk. The objective of this paper is to assess associations between GI or GL and lung cancer and its histologic subtypes (i.e., squamous cell lung carcinoma, lung adenocarcinoma, large cell lung carcinoma, small cell lung carcinoma) using data from a population-based case-control study in Los Angeles County.

METHODS

Study population

The newly diagnosed lung cancer cases and population-based cancer-free controls were recruited from Los Angeles County between 1999 and 2004. Detailed descriptions of the participant recruitment and data collection for the study have been described elsewhere in previous publications [28, 29]. In brief, all participants were residents of Los Angeles County at the time of diagnosis for cases or recruitment for controls, ranged in age from 18 to 65 years old during the enrollment period, and spoke English, Spanish, or had translators available at home. Histologically confirmed incident cancer cases of lung and upper aero-digestive tract (UADT) were recruited through the rapid ascertainment system of the University of Southern California (USC) Cancer Surveillance Program for Los Angeles County. Controls were originally matched to cases by age (within 10-year intervals), sex, and neighborhood of residence. The original study identified 1,556 lung cancer cases, 1,301 UADT cancer cases and 1,321 cancer-free controls. The current study focuses on lung cancer only. Among all eligible subjects, the participation rates were 39% (611 of 1,556) for lung cancer and 79% (1,040 of 1,321) for controls [28]. For the eligible lung cancer cases who did not participate in this study, half of them either died (N= 389) or were too ill to participate (N= 78). We excluded 9 lung cancer cases and 8 controls with missing information on GI or GL value, and 9 lung cancer cases and 6 controls with missing or implausible (<500 or >5,500 kcal/day) non-alcohol energy intake (Figure 1). In addition, the matches were broken and controls for both lung and UADT cancer cases were included in the current analyses in order to increase power in our analyses. A total of 593 lung cancer cases and 1,026 controls were in the final analyses. The study was approved by the Institutional Review Boards (IRBs) of the University of California at Los Angeles and USC; all participants provided written informed consent.

Specification of variables

In-person interviews were conducted by trained study staff using questionnaires to collect information on demographic factors, detailed dietary history, as well as detailed histories of tobacco smoking (cigarette, cigar, and pipe) and alcohol consumption, occupational and environmental exposures, and medical history. Measures of dietary intake were derived from a 78-item semi-quantitative FFQ based on the validated Brief Block FFQ [30]. Food sources in the FFQ included fruits, vegetables, meat and mixed dishes, starches and salty snacks, breakfast foods, sweets and dairy products (see Supplementary Table 1 for the corresponding food items). Participants were queried about their usual frequency of

consumption over the previous year - rarely/never, per year, month, week, or day. Portion sizes were measured in teaspoons, tablespoons, ounces, pounds, cups, pieces, handfuls, pats, burritos, patties, bowls, and slices for solid food items and as number of cups, ounces, or glasses consumed for drinks. The reference period of the dietary intake was 1 year before diagnosis for cases and 1 year before the interview for controls.

Food frequency was converted to daily intake in grams for each food item by linking portion size and frequency in our FFQ with data from the USDA Nutrient Database Standard Reference, version 16 (SR16)[31]. This document provides the grams per portion size as well as the nutritional composition for each food item. We linked GI values (using a scale assuming pure glucose=100) to each food item using the published GI estimates. We searched for the most similar food item within the international GI tables [32, 33], considering only studies in healthy subjects and conducted in the United States or Canada. Whenever more than one GI value was provided for the same type of food in the international table, the average GI value was assigned to that food item. When the food item could not be found in the tables, we then searched the GI values compiled by Flood et al. [34]. The process of linkage was carried out by manually reviewing the GI tables to identify the best matches for each food item in the questionnaire.

Average dietary GI for each participant was calculated by summing the products of the GI value and the available carbohydrates of each food item consumed per day, then dividing by the total amount of available carbohydrates consumed per day [12, 24]. Average dietary GI was calculated as below:

$$\begin{aligned} &Average\ dietary\ GI \\ &= \frac{\sum(GI\ of\ each\ food\ item\ *\ available\ grams\ of\ carbohydrate\ intake\ of\ each\ food\ item)}{total\ available\ grams\ of\ carbohydrate\ intake} \end{aligned}$$

where summation is across all foods eaten by the individual. Grams of available carbohydrates consumed per day, including starch and sugars, were calculated by subtracting dietary fiber from total carbohydrates.

Daily GL was calculated by summing the products of the GI for each food consumed and the grams of available carbohydrates of that food item consumed per day, divided by 100 [6, 35, 36]. The formula of daily GL was as below:

$$Daily\ GL = \frac{\Sigma(GI\ of\ each\ food\ item\ *\ available\ grams\ of\ carbohydrate\ intake\ of\ each\ food\ item)}{100}$$

where summation is across all foods consumed by the individual. Each GL unit represents the effect of consuming one gram of carbohydrate from glucose. The distribution of GI and GL in the control group was used to determine the cut-off points for tertile categories.

Statistical analysis

Unconditional logistic regression was used to estimate adjusted odds ratios (OR) and 95% confidence intervals (95% CI). The following covariates were included in the models to adjust for potential confounders: age (continuous), sex (categories shown in Table 1), race/

ethnicity (Caucasian, Hispanic, Black, others), education years (continuous), body mass index (BMI, continuous), tobacco smoking duration (continuous), tobacco smoking frequency (continuous), and alcohol drinking frequency (continuous). For GI, models were additionally adjusted for energy intake without alcohol (continuous); for GL, models were further adjusted for energy intake without alcohol and available carbohydrates (continuous) to avoid the collinearity between GL and available carbohydrates. We used tobacco smoking duration and frequency instead of tobacco packyears to control the effect of tobacco smoking on lung cancer risk because packyear is a relatively crude way for the adjustment [37]. For example, an individual who smoked 0.5 pack per day for 10 years and an individual who smoked 5 packs per day for one year had five packyears, but their lung cancer risk may be different. P_{trend} was estimated for a dose-response association by testing the linear trend between lung cancer risk and the levels of exposure of interest.

The associations between daily GI and GL intake and histologic subtypes of lung cancer were also evaluated. Stratified analyses were performed to evaluate the association between GI and GL and lung cancer in smoking status, BMI, and diabetes history. We also stratified by GL (<110 or >=110) when the exposure of interest was GI, and by GI when the exposure of interest was GL (GI <55 or >=55). The cut-off points were decided by considering the distribution among controls and the suggestion from previous studies [38, 39]. $P_{interaction}$ was estimated by the p-value of the product-term between exposure of interest and the stratified factor. Three sensitivity analyses were conducted to ensure the robustness of our results: 1) we restricted the population with no diabetes history, 2) we used tobacco packyears instead of tobacco smoking duration and tobacco smoking frequency as a covariate, 3) we included more covariates in the statistical model to ensure the associations were robust. The variables we used included: secondhand smoking, vitamin intake, and snuff use. All analyses were performed using the SAS system, version 9.4 (SAS Institute, Cary, NC).

RESULTS

Of 593 lung cancer cases and 1,026 controls, the distribution of cases and controls across categories of selected demographic characteristics and potential confounding factors is summarized in Table 1. Compared to controls, cases were older, more female, and had a lower education level, a higher frequency of tobacco smoking and alcohol drinking, a lower proportion of overweight and obese individuals (p for chi-square < 0.001, Table 1). There was no difference in diabetes history between cases and controls. Characteristics of lung cancer cases by subtypes were showed in Supplementary Table 2. Consistent with the previous finding, adenocarcinoma cases were younger, more female and never-smokers compared to other subtypes (Supplementary Table 2).

The highest GI tertile category (T3) was associated with a higher lung cancer risk ($OR_{T3\ vs.\ T1}$=1.62; 95% CI= 1.17–2.25, P_{trend}=0.004, Table 2). Across lung cancer histologic subtypes, high dietary GI was associated with an increased risk of lung adenocarcinoma ($OR_{T3\ vs.\ T1}$=1.82; 95% CI= 1.22–2.70, P_{trend}=0.003) and small cell lung carcinoma ($OR_{T3\ vs.\ T1}$=2.68; 95% CI= 1.25–5.74, P_{trend}=0.009). Little association between GL and lung cancer risk was observed ($OR_{T3\ vs.\ T1}$=1.13; 95% CI= 0.79–1.64,

P_{trend}=0.471). The inference remained the same in the sensitivity analyses when using tobacco packyears as a covariate or adding secondhand smoking, vitamin intake, and snuff use in the model (data not shown). When we restricted the analyses to individuals with no diabetes history, the inference remained the same as well (Supplementary Table 3).

In the stratified analyses, the positive association between high GI and lung cancer risk was observed among ever-tobacco-smokers ($OR_{T3\ vs.\ T1}$=1. 92; 95% CI= 1.35–2.74, P_{trend} <0.001, Table 3), individuals with BMI <25 ($OR_{T3\ vs.\ T1}$=2.18; 95% CI= 1.28–3.72, P_{trend} =0.004), and individuals with no diabetes history ($OR_{T3\ vs.\ T1}$=1.63; 95% CI= 1.15–2.31, P_{trend} =0.005). When we further stratified by daily GL, an increased risk of lung cancer for high dietary GI was observed when individuals had daily GL <110 ($OR_{T3\ vs.\ T1}$=2.31; 95% CI= 1.41–3.80, P_{trend}=0.001, Table 3).

DISCUSSION

In this population-based case-control study, we found that high average dietary GI was positively associated with lung cancer risk, and this association was stronger in ever smokers and individuals with low daily GL, BMI <25, and no diabetes history. The risk of overall lung cancer or its histologic subtypes was not associated with GL.

High dietary GI may contribute to cancer development through hyperglycemia-induced overproduction of oxidative stress or inflammation [40, 41] and glycolysis-linked activation of oncogenic pathways [42]. A hospital-based case-control study with 463 lung cancer cases and 465 controls in Uruguay reported a positive association between high dietary GI and lung cancer risk[25]. Melkonian et al. reported a positive association between dietary GI and lung cancer among non-Hispanic whites, including 1,905 lung cancer cases and 2,413 controls [23]. Null associations between dietary GI, GL and lung cancer from a prospective National Institutes of Health (NIH)–AARP Diet and Health Study, a Canadian nationwide population-based case–control study and a prospective Shanghai Women's and Men's Health Study have been reported [24, 26, 27]. In the current study, we observed that high dietary GI was associated with an elevated lung cancer risk. Additionally, among individuals who consumed daily GL <110, high dietary GI was associated with increased lung cancer risk, indicating the food choice could be important for people who eat less. High GI and GL diet stimulate insulin release and increase glucose uptake, and have been hypothesized to link with cancer development [38, 40, 41]. High blood glucose concentration stimulates insulin release and elevates the bioavailability of IGF-1, which plays an important role in carcinogenesis [43]. IGF-1 is involved in regulating cell proliferation and differentiation and has been detected at higher plasma levels in lung cancer cases than in controls [44]. Onodera et al. found in their cell-based study that sugar uptake may promote oncogenesis by activating the HIF-1, AMPK or mTOR oncogenic pathways [42]. Furthermore, hyperglycemia due to sustained high sugar consumption can upregulate O-GlcNAcylation which enhances the anchorage-independent growth in lung cancer cells [45–47].

Inconsistent associations of GI and GL with lung cancer risk may be partly due to differences in underlying dietary patterns. That is, higher dietary GL is strongly associated with higher carbohydrate intake, while a higher GI is also associated with lower intakes of

dairy products, legumes, fruit and vegetables [48]. In line with this hypothesis, a Netherlands case-cohort study including 1,426 lung cancer cases showed a positive association of lung cancer with a "*pork, processed meat, and potatoes pattern* dietary pattern, which was simultaneously based on high-GI (e.g. potatoes) and low-GL (e.g. pork and processed meat) foods [49]. Thus, it suggests that the positive association between dietary GI and lung cancer risk may be confounded by the consumption of nutrients other than carbohydrates. In addition, an increased risk of lung cancer was associated with high GI when the individuals had low daily GL (GL <110) in our stratified analyses.

We observed that high GI was associated with increased risks of adenocarcinoma and small cell lung carcinoma. Previous studies suggested that the impact of dietary factors, such as fruit, vegetable, and Vitamin D, was different by subtypes [23, 50, 51]. Cheng et al. reported that the protective effect of vitamin D intake was more pronounced in adenocarcinoma among never smokers but not with other histologic types of lung cancer [51]. Although the inference remained the same when adjusted for vitamin intake in the model, we cannot rule out the influence of the complicated food intake. Individuals who had lower GI may consume more food items with higher vitamin D which was inversely associated with adenocarcinoma [23]. Adenocarcinoma cases had the highest proportion of never smokers (26.0%) and small cell carcinoma cases had the lowest proportion of never smokers (5.6%), compared with other histologic subtypes in our study. Tobacco smoking has been associated with the expression of IGF-1 and its receptor which may partially explain the association among high GI, small cell lung carcinoma, and ever smokers in our analyses [52, 53]. Future research is needed to elucidate the biological mechanisms on the interplay between smoking, food intake, GI, and risk of lung cancer histologic subtypes.

Although insulin resistance and impaired insulin secretion are common in individuals with diabetes or obesity [54], we did not observe an increased risk among individuals with diabetes history or BMI>=25 in the stratified analyses. The statistical power was limited for diabetes history since only 42 cases had diabetes before cancer diagnosis. It is unclear why the association between high GI and lung cancer risk only appeared among individuals with BMI <25. It could be possible that individuals with normal BMI or underweight were more susceptible to the impact of GI.

A limitation of our study is that recall bias may have influenced the results if cases recalled more details of high GI food intake. However, GI and GL was not a known risk factor during the recruitment period, thus it is less likely to influence our conclusion. Since nutritional components for each food item were measured at a single time point. If GI and GL were overestimated, it would lead the bias toward the null. It was unlikely to avoid unmeasured or uncontrolled confounding in the current study, such as missing physical activity. If individuals with high physical activity tended to have high GI and GL intake and low lung cancer risk, we might underestimate the association. Lastly, the current analyses may have non-differential misclassification of GI and GL since they were measured from the self-report FFQ. Thus, we might underestimate the association among GI, GL, and lung cancer.

The major strength of this study is that we obtained a comprehensive assessment of sociodemographic and lifestyle characteristics by questionnaires which allowed us to

estimate dietary effects and adjust for potential confounders, including tobacco smoking duration and frequency and diabetes history.

In conclusion, findings from this population-based case-control study support a positive association of average dietary GI on the risk of lung cancer. Our results may be informative for policy-making and program planning for lung cancer prevention. A better understanding of dietary factors and how they influence established risk and preventative factors is paramount to understanding lung cancer etiology to provide effective prevention strategies and to reduce lung cancer incidence for public health promotion. Further research with better dietary GI assessment is necessary to replicate these findings and to better understand the underlying mechanisms linking GI /GL and lung cancer in humans.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- Glycemic index was associated with increased lung cancer risk
- Positive associations of glycemic index on adenocarcinoma and small cell carcinoma
- Stronger associations in individuals who had smoked, BMI <25, and no diabetes history

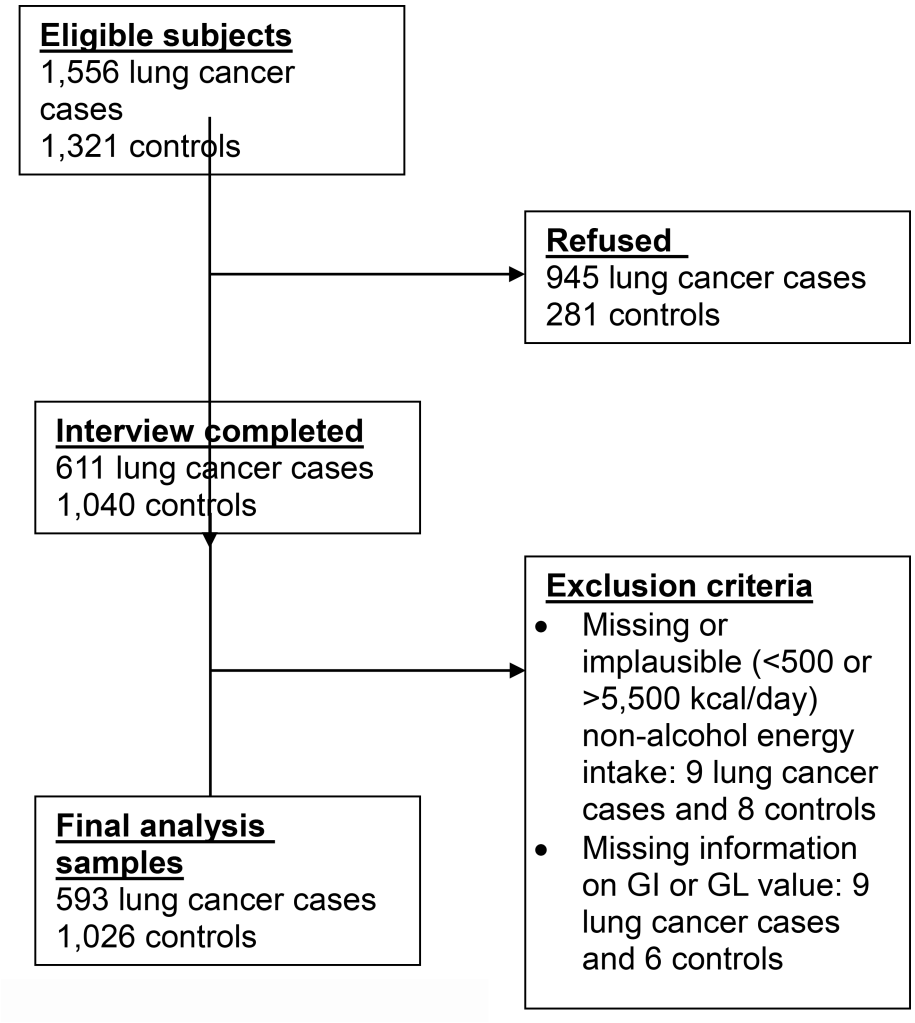

Figure 1.
Flow chart showing study population and exclusion criteria

Table 1.

Characteristics of lung cancer cases and controls in the LA case-control study

	Lung cancer cases, n(%) n=593	Controls, n(%) n=1026	P for chi- square
Age(years)			<0.001
<45	59 (9.9)	221 (21.5)	
45–54	291 (49.1)	491 (47.9)	
55+	243 (41.0)	314 (30.6)	
Sex			<0.001
Male	297 (50.1)	616 (60.0)	
Female	296 (49.9)	410 (40.0)	
Race/Ethnicity			<0.001
Caucasian	350 (59.0)	631 (61.5)	
Hispanic	68 (11.5)	200 (19.5)	
Black	93 (15.7)	98 (9.6)	
Asian	66 (11.1)	60 (5.8)	
Other	15 (2.5)	36 (3.5)	
Missing	1 (0.2)	1 (0.1)	
Education (years)			<0.001
0–12	255 (43.0)	295 (28.8)	
13–16	268 (45.2)	474 (46.2)	
17+	70 (11.8)	256 (25.0)	
Missing	0 (0)	1 (0.1)	
Tobacco smoking frequency (cigarettes-equivalent/day)			<0.001
0	107 (18.0)	469 (45.7)	
>0 to 10	58 (9.8)	237 (23.1)	
>10 to 20	199 (33.6)	204 (19.9)	
>20	229 (38.6)	116 (11.3)	
Tobacco smoking duration (years)			<0.001
0	107 (18.0)	469 (45.7)	
>0 to 10	18 (3.0)	146 (14.2)	
>10 to 20	37 (6.2)	135 (13.2)	
>20	431 (72.7)	276 (26.9)	
Alcohol drinking frequency (drinks/day)			<0.001
0	163 (27.5)	257 (25.0)	
>0 to <1	211 (35.6)	486 (47.4)	
1 to <3	130 (21.9)	192 (18.7)	
3 to <5	45 (7.6)	45 (4.4)	
5+	43 (7.3)	43 (4.2)	
Missing	1 (0.2)	3 (0.3)	
Diabetes history			0.507
Yes	42 (7.1)	82 (8.0)	
No	551 (92.9)	944 (92.0)	

	Lung cancer cases, n(%) n=593	Controls, n(%) n=1026	P for chi- square
Body Mass Index (BMI)			<0.001
Underweight (<18.5)	18 (3.0)	13 (1.3)	
Normal (18.5 to <25)	254 (42.8)	354 (34.5)	
Overweight (25 to <30)	210 (35.4)	398 (38.8)	
Obese (30+)	110 (18.5)	259 (25.2)	
Missing	1 (0.2)	2 (0.2)	

Table 2.

Odds ratio (OR)[a] and 95% confidence interval (CI) of glycemic index and glycemic load on lung cancer and the subtypes

	Controls	Lung cancer cases		Squamous cell lung carcinoma		Lung adenocarcinoma		Large cell lung carcinoma		Small cell lung carcinoma	
	n (%)	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Glycemic Index[b]											
T1	341 (33.2)	142 (23.9)	Reference	20 (22.5)	Reference	74 (25.3)	Reference	25 (22.3)	Reference	15 (21.1)	Reference
T2	343 (33.4)	185 (31.2)	1.29 (0.93, 1.77)	29 (32.6)	1.05 (0.53, 2.11)	88 (30.1)	1.25 (0.85, 1.84)	39 (34.8)	1.52 (0.82, 2.81)	20 (28.2)	1.58 (0.72, 3.48)
T3	342 (33.3)	266 (44.9)	1.62 (1.17, 2.25)	40 (44.9)	1.33 (0.67, 2.64)	130 (44.5)	1.82 (1.22, 2.70)	48 (42.9)	1.64 (0.87, 3.09)	36 (50.7)	2.68 (1.25, 5.74)
P_{trend}			0.004		0.388		0.003		0.140		0.009
Glycemic load[c]											
T1	342 (33.3)	185 (31.2)	Reference	28 (31.5)	Reference	98 (33.6)	Reference	31 (27.7)	Reference	22 (31.0)	Reference
T2	343 (33.4)	201 (33.9)	1.25 (0.92, 1.71)	27 (30.3)	0.99 (0.51, 1.95)	103 (35.3)	1.29 (0.89, 1.86)	39 (34.8)	1.61 (0.89, 2.92)	22 (31.0)	1.46 (0.70, 3.04)
T3	341 (33.2)	207 (34.9)	1.13 (0.79, 1.64)	34 (38.2)	0.87 (0.39, 1.92)	91 (31.2)	1.15 (0.73, 1.81)	42 (37.5)	1.38 (0.67, 2.84)	27 (38.0)	2.07 (0.89, 4.78)
P_{trend}			0.471		0.729		0.498		0.360		0.090

[a] Models adjusted for age, sex, race/ethnicity, education, energy intake, BMI, tobacco smoking duration, tobacco smoking frequency, alcohol drinking frequency.

[b] The range for glycemic index tertiles: T1, 24.50–51.68; T2, 51.69–56.56; T3, 56.57–68.88.

[c] The range for glycemic load tertiles: T1, 9.10–89.07; T2, 89.08–141.33; T3, 141.34–547.53.

Table 3.

Odds ratio (OR)[a,b] and 95% confidence interval (CI) of glycemic index and glycemic load on lung cancer in strata of selected covariates

	T1	T2	T3	P_{trend}	$P_{interaction}$
Glycemic Index					
Tobacco smoking status					0.972
Never-smokers	Reference	1.13 (0.62, 2.04)	1.24 (0.65, 2.35)	0.518	
Ever-smokers	Reference	1.39 (0.98, 1.97)	1.92 (1.35, 2.74)	<0.001	
BMI					0.166
<25	Reference	1.31 (0.79, 2.17)	2.18 (1.28, 3.72)	0.004	
>=25	Reference	1.32 (0.87, 2.00)	1.34 (0.88, 2.05)	0.200	
Diabetes history					0.570
No Diabetes	Reference	1.24 (0.89, 1.74)	1.63 (1.15, 2.31)	0.005	
Diabetes	Reference	2.10 (0.69, 6.39)	1.35 (0.44, 4.08)	0.646	
Glycemic load					0.123
<110	Reference	1.31 (0.88, 1.96)	2.31 (1.41, 3.80)	0.001	
>=110	Reference	0.90 (0.48, 1.69)	1.06 (0.57, 1.96)	0.576	
Glycemic Load					
Tobacco smoking status					0.561
Never-smokers	Reference	1.00 (0.56, 1.77)	0.62 (0.29, 1.31)	0.241	
Ever-smokers	Reference	1.17 (0.83, 1.64)	1.31 (0.88, 1.95)	0.182	
BMI					0.849
<25	Reference	1.43 (0.87, 2.34)	1.18 (0.63, 2.19)	0.540	
>=25	Reference	1.16 (0.77, 1.74)	1.11 (0.70, 1.76)	0.653	
Diabetes history					0.146
No Diabetes	Reference	1.18 (0.85, 1.63)	1.03 (0.70, 1.51)	0.853	
Diabetes	Reference	1.82 (0.60, 5.48)	2.32 (0.57, 9.43)	0.222	
Glycemic index					0.274
<55	Reference	0.99 (0.66, 1.49)	1.00 (0.53, 1.91)	0.997	
>=55	Reference	1.15 (0.65, 2.04)	0.85 (0.47, 1.55)	0.375	

[a] Models adjusted for age, sex, race/ethnicity, education, energy intake, BMI, tobacco smoking duration, tobacco smoking frequency, alcohol drinking frequency.

[b] The range for glycemic index: T1,24.50–51.68; T2, 51.69–56.56; T3, 56.57–68.88. The range for glycemic load: T1,9.10–89.07; T2, 89.08–141.33; T3, 141.34–547.53.