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Dietary total antioxidant capacity and odds of lung cancer: a large case-control study

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Abstract

Background& aims We aimed to study the association between dietary total antioxidant capacity (dTAC) and lung cancer (LC) odds in an Iranian population.

Methods We recruited histopathologically diagnosed LC patients and healthy subjects from 10 provinces of Iran. Trained interviewers conducted face-to-face interviews using a structured questionnaire to collect demographic and other non-dietary information. Dietary habits in the previous year were evaluated using a validated food frequency questionnaire (FFQ). We calculated daily energy and nutrient intakes using the USDA Food Composition Table. DTAC was assessed as ferric reducing antioxidant power (FRAP) and total radical-trapping antioxidant parameters (TRAP) whose scores were calculated using published databases. The odd ratios (OR) of LC and 95% confidence intervals (CI) were estimated using unconditional logistic regression after adjusting for potential confounders. Moreover, we assessed the associations in stratified groups of age, gender, tobacco including waterpipe smoking, and opium use.

Results Six hundered and sixty patients and 3,412 healthy controls were included in our study. Higher FRAP and TRAP scores were associated with a lower odd of LC (FRAP, upper tertile (T3) vs. lower tertile (T1): OR = 0.53, 95% CI: 0.40–0.68; TRAP, T3 vs. T1: OR = 0.44, 95% CI: 0.33–0.57) with a significant dose-response trend for both scores ($p < 0.01$). The inverse association was seen for both indicators in all histologic types of LC and in all stratified analyses including male/female, tobacco smokers/nonsmokers, opium users/nonusers, water pipe users/nonusers, and subjects under/over 50 years of age. However, Interaction between none of these variables with dTAC scores was significant.

Conclusion Higher dTAC is associated with a lower odd of LC. The strong association in all subgroups highlights the importance of an antioxidant-rich diet intake in all subjects, even in the low-risk group.

Highlights

- Lung cancer (LC) is the most common cancer among males and the third most common cancer among females worldwide. Focusing on primary prevention may be the main strategy for reducing the overall mortality of LC, especially in LMICs.

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- This study showed that dTAC assessed either by FRAP or TRAP procedure is inversely associated with the odds of LC. The strong association in all subgroups, emphasizes the importance of an antioxidant-rich diet in all subjects even in nonsmokers with a lower odds of lung cancer.

Introduction

Lung cancer (LC) is the most common cancer among males and the third most common cancer among females worldwide [1]. LC is estimated to be the leading cause of cancer-related deaths. One out of every ten cancer diagnoses and one out of every five cancer deaths are attributed to LC [1, 2]. Its prevalence has decreased in most high-income areas, primarily due to a decrease in smoking [1, 3]. Unfortunately, about 58% of LC incidence occurs in low- and middle-income countries (LMICs) [1]. They are mainly diagnosed in late stages, and 5-year survival is only 10–20% in most regions [1]. Even with joint efforts for early detection and effective therapeutic procedures, the survival rate is still disappointing. Focusing on primary prevention may be the main strategy for reducing the overall mortality of LC, especially in LMICs [4]. All mentioned highlighting the importance of a better understanding of LC risk factors to develop effective prevention strategies, particularly in LMICs.

Several studies have examined LC risk factors. Smoking is known as a major risk factor, responsible for two-thirds of the incidence of LC worldwide. Occupational exposures, outdoor and indoor air pollution, and exposure to radon decay products are other important risk factors. There is evidence that dietary factors such as red meat, alcoholic beverages, fruits, and vegetables are associated with the risk of LC. In several studies, some antioxidants such as retinol, beta-carotene, carotenoids, vitamin C, and isoflavones have been associated with a reduced risk of LC. However, a comprehensive review of the evidence by the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) concluded that there is limited evidence on the association between LC risk and dietary factors [5].

It has been claimed that antioxidants can reduce the risk of cancers by regulating redox status, preventing carcinogen formation, and inhibiting biological oxidation [6]. However, studies on the association between single antioxidants or supplementation with the risk of cancers have given contrasting results [7, 8]. Some studies have shown that the parallel consumption of antioxidants reduces the risk of cancer significantly more than each antioxidant alone [9]. Studies show that antioxidants have different chemical reactions and redox potentials and synergistically interact against oxidative stress [10, 11].

Dietary total antioxidant capacity (dTAC) is an index that determines the whole antioxidant capacity of a diet. The most common approaches to assess dTAC are ferric reducing antioxidant power (FRAP) and total radical-trapping antioxidant parameters (TRAP), which measure the reducing power and the chain-breaking antioxidant capacity, respectively. Several studies have examined the association between these dietary scores and the risk of gastric, colorectal, breast, pancreatic, and endometrial cancers [12–15], and some studies investigated the association between individual antioxidant intake and the risk of LC [4, 16, 17]. However, there are no studies on the association between dTAC and the risk of LC. In several studies, the association between dietary factors and LC risk was different in cigarette smokers and nonsmokers [5]. We aim to study the association between dTAC in terms of FRAP and TRAP with the odds of LC regarding their cigarette smoking status.

Materials & methods

Settings

This study was conducted using data from the IROPICAN study. The methodological details of that study have been described previously [18]. In brief, the IROPICAN study is a large multicenter case-control study evaluating the association between opium use and the odds of lung, bladder, head and neck, and colorectal cancers. we recruited newly histopathologically diagnosed cancer patients and healthy hospital visitors as controls from 10 provinces in the east, south, north, and centre of Iran. The pathological reports and morphology codes in the patient's medical record were used to allocate ICD-O3 codes.

For each cancer case in our study, we included controls from the same province, sex, and age group after every ten cases. It is essential to highlight that our study covered multiple types of cancers, and we used data from control subjects across these diverse cancer types for this paper. Consequently, we adjusted our analysis for age, sex, and provinces.

patients with a secondary cancer diagnosis were not included in this study. The control group consisted of healthy visitors who came to visit patients with no cancer diagnosis. We asked all participants to complete a questionnaire, particularly a Food Frequency Questionnaire (FFQ), based on their habits in the previous year. Patients were particularly asked to recall their habits before their cancer diagnosis. Trained interviewers conducted face-to-face interviews using a structured questionnaire to obtain demographic and other non-dietary data. A detailed description of the questionnaire and computing-related scores were described previously [19]. Briefly, socioeconomic status (SES) was determined using principal component analysis by combining some data related to education, income, and home appliances. Physical activity workload (PPWL) was estimated based on the Finnish Job Exposure Matrix (fINJEM)) [20].

Assessment of dTAC scores

Dietary habits over the last year were assessed using a validated Food Frequency Questionnaire (FFQ). The full description of the FFQ and its validation process was provided elsewhere [21, 22]. Briefly, it is a quantitative 131-food itemized questionnaire, which asks the frequency of food consumption in year/season/ month or week. Moreover, it asks the amount of consumption based on household measures of foods. Interviewers asked the patients to recall their dietary habits a year before the appearance of symptoms of the disease. We calculated the daily intake of each food and then converted it to energy and nutrient intake using the USDA food composition Table [23]. We asked about supplement use in FFQ, but the frequency of consumption was too small, so we did not consider supplements in any analysis.

Data on dTAC scores was gathered from published databases. These databases measured the TRAP capacity and FRAP of foods by measuring the chain-breaking antioxidant capacity and the ferric-reducing power, respectively [24, 25]. Then, dTAC values were computed for each participant considering the daily intake of food items multiplied by corresponding FRAP or TRAP values. The dTAC values of the nearest comparable foods were considered for food items without dTAC value in those databases. Computing energy, nutrients, and dTAC values were done in access software (Microsoft Access 2010) using the USDA food composition Table [26].

Statistical analysis

The TRAP and FRAP scores were adjusted for energy intake using the residual method [27, 28]. Subjects with energy intake under 500 and over 4500 Kcal/d (±3SD) were omitted and considered as under and over-reporting. This resulted in a reduction of 8 (1.2%) cases and 61(1.7%) controls. Then, participants were categorized to tertile of dTAC scores based on the distribution of the dTAC scores in the control group.

OR and 95% CI were estimated using unconditional logistic regression after adjusting for energy (continues, Kcal/d), province (nine provinces of Iran), age (five categories), and gender (male/female) in the first model (model A). Further adjustment for SES (low, medium, high), opium use (yes, no), cigarette smoking (no, yes), water pipe use (no, yes), regular alcohol use (no, yes), perceived workplace physical activity (sedentary, moderate, heavy, unknown) and BMI (continues, kg/m^2) was done in a second model (model B). We used the median value of TRAP or FRAP as a continuous variable in unconditional logistic models to test for the P-value for the trend.

Stratified analyses were conducted based on cigarette smoking status (smokers/non-smokers), the histopathological subtype of LC (small cell carcinoma, adenocarcinoma, and squamous cell carcinoma), gender (male/female), age (=<50 / >50 years old). As tobacco use is the predominant cause of LC, odd ratios (OR) for LC risk across the level of FRAPS and TRAPS among smokers and non-smokers, opium users/nonusers, and water pipe users/nonusers are also reported. Nonusers in all three analyses did not use cigarettes, water pipes, or opium. We considered cigarette smokers with low dTAC scores as a reference group to the effect of increasing dTAC. An interaction term was incorporated into the models to assess the interaction between smoking status and dTAC tertile concerning the odds of lung cancer (LC). The P-value for interactions was determined using the likelihood ratio test. The same method was used to assess the interaction between gender, age, physical activity, opium use, and water pipe use with dTAC scores on the odds of LC. All statistical analysis was done in STATA software (Stata 14.1, College Station, Texas 77845 USA). Two-sided Pvalue < 0.05 were considered statistically significant.

Results

A total of 627 cases and 3477 healthy controls were recruited from May 2017 to July 2020 in our study. Among them, 7 were omitted because of incomplete questionnaires. Eight individuals from the 624 cases and 61 individuals from the 3473 controls were excluded due to over- or under-reporting of energy intake. Almost two-thirds of our participants were male in both case and control groups. The proportions of smoking (63% vs. 28%), opium use (48% vs. 13%), water pipe use (11% vs. 7%), and regular alcohol use (10% vs. 4%) were higher in cases comparing to controls (Table 1). Intake of energy, vegetables, fruits, total meat, and red meat was not different between cases and controls (Table 2).

The main contributors to dTAC in our control group were cereals (33.9% for FRAP and 59.9% for TRAP). Other sources of FRAP and TRAP in our control group were fruits (29.9% and 8%, respectively), vegetables (17.8% and 30.9%), legumes (4.3% and 0.98%), nuts (2.9% and 3.7%), sweets (1.0% and 3.2%) and fruit juice (3.2% and 1.0%). Dairy products (7.6%) and vegetable oils (1.2%) were minor sources of the FRAP. More details of this contribution were reported elsewhere [29]. The Pearson correlation between TRAP and FRAP scores was 0.36 in the control group ($P < 0.001$).

The associations between dTAC and the odds of LC in the total population and by subtype of LC are outlined in Table 3. Individuals in the highest tertile of the

Table 1 Characteristics of lung cancer patients and controls in a large case/control study in Iran[1]

Characteristics		Cases (*n*=616)	Controls (*n*=3,412)	*p*-value[2]
Gender	male	474(77)	2,355(69)	< 0.001
	female	142(23)	1,057(31)	
Socioeconomic status	Low	265(43)	954(28)	< 0.001
	Median	221(36)	1,145(34)	
	High	130(21)	1,313(38)	
Opium use	No	318(52)	2,956(87)	< 0.001
	Yes	298(48)	456(13)	
Cigarette smoking	No	230(37)	2,451(72)	< 0.001
	Yes	386(63)	961(28)	
Water pipe use	No	548(89)	3,187(93)	< 0.001
	Yes	68(11)	225(7)	
Regular alcohol use	No	557(90)	3,270(96)	< 0.001
	Yes	59(10)	142(4)	
Work Physical activity	Sedentary	177(29)	1,106(32)	< 0.001
	Moderate	133(22)	743(22)	
	Heavy	197(32)	746(22)	
	Unknown	109(18)	817(24)	
Province	Tehran	129(21)	813(24)	< 0.001
	Fars	190(31)	933(27)	
	Kerman	110(18)	523(15)	
	Golestan	47(8)	364(11)	
	Mazandaran	33(5)	132(4)	
	Kermanshah	38(6)	249(7)	
	Khorasan-Razavi	6(1)	162(5)	
	Bushehr	33(5)	67(2)	
	Hormozgan	16(3)	73(2)	
	Systan-Baluchestan	14(2)	96(3)	
Age category	30–39	13(2)	252(7)	< 0.001
	40–49	72(12)	548(16)	
	50–59	203(33)	1054(31)	
	60–69	213(35)	1073(31)	
	≥ 70	115(19)	485(14)	
BMI (kg/m^2, mean ± SD)		25.3 ± 5.3	26.7 ± 4.8	< 0.001

[1]reported figures are number and percent unless indicated

[2]Obtained from chi-square test for categorical variables and independent student's t-test for continuous variables

FRAP score had almost 50% lower odds of LC compared to those who were in the lowest tertile of the FRAP (OR=0.53, 95% CI: (0.40–0.68); P for trend<0.001). When patients were stratified by lung cancer histological subtypes, odds reduction was observed across all subgroups. The most substantial odds reduction occurred in squamous cell LC (OR=0.45, 95% CI: 0.28–0.73). However, the differences in the association between dTAC scores and lung cancer subtypes were not statistically significant.

Similar trends were observed in TRAP scores. The odds of LC were 60% lower in the third tertile vs. the first tertile (OR=0.44, 95% CI: 0.33–0.57); P for trend=0.002). This score showed the highest risk reduction in small cell cancer for those in the third tertile of TRAP score compared to the first tertile (OR=0.35, 95%CI: 0.19–0.62) with a significant dose-response trend (P for trend=0.001). The association of TRAP and odds of LC were not significant in adenocarcinoma and other subtype of LC. This inverse association is also significant in continuous models in LC without considering subtypes (OR=0.67, 95% CI: 0.58–0.77 for FRAP and OR=0.71, 95% CI: 0.61–0.83 for TRAP).

In stratified analyses, inverse associations were found in both men and women, water pipe users and nonusers, opium users and non-users, and subjects under and over 50 years of age. However, the interaction terms between gender, water pipe use, and age with dTAC scores were not significant. The results of age or gender interaction analyses are not reported in detail. As tobacco exposure is the predominant cause of LC, OR for LC odds across the level of FRAP and TRAP among smokers and

Table 2 Intake of antioxidant food sources and nutrients of lung cancer patients and controls in a large case/control study in Iran[1]

	patients (*n* = 616)	Controls (*n* = 3,412)	*p*-value
Energy (kcal/d, mean ± SD)	1761.9 ± 750.5	1850.6 ± 680.9	
Grains (g/day)	484.4 ± 265.2	493.2 ± 268.1	0.456
Vegetables (g/day)	442.7 ± 373.6	423.2 ± 244.3	0.096
Fruits (g/day)	358.5 ± 258.0	363.0 ± 293.6	0.721
Juice (g/day)	9.1 ± 21.9	9.4 ± 26.9	0.759
Total meat (g/day)	65.7 ± 45.3	67.1 ± 49.9	0.511
Red meat (g/day)	21.7 ± 24.4	22.8 ± 27.2	0.357
Dairy (g/day)	65.7 ± 45.3	67.1 ± 49.9	0.442
Beans (g/day)	32.9 ± 43.8	31.3 ± 29.9	0.235
Nuts (g/day)	6.2 ± 5.6	5.9 ± 5.6	0.389
Confectionary (g/day)	38.4 ± 37.6	36.9 ± 34.7	0.340
Vegetable oils (g/day)	17.8 ± 14.3	17.8 ± 14.3	0.931
Vitamin C (mg/day)	69.1 ± 50.2	79.5 ± 50.2	< 0.001
Alpha Tocopherol (µg/d)	7.2 ± 3.9	7.7 ± 4.2	0.015
Beta Tocopherol (µg/d)	0.16 ± 0.14	0.17 ± 0.14	0.260
Alpha Carotene (µg/d)	125.2 ± 100.9	142.6 ± 120.2	0.001
Beta Carotene (µg/d)	2102.4 ± 200.6	2363.2 ± 1707.1	0.001
Lycopene (µg/d)	4668.4 ± 3982.9	5291.4 ± 4629.2	0.002
Selenium (mg/d)	65.2 ± 30.5	72.2 ± 33.0	< 0.001

[1]reported figures are mean ± SD of gram/day of intakes unless defined

[2]Obtained from independent student's t-test

non-smokers is displayed in Supplementary Table 1. Moreover, the interaction between opium or water pipe use, and dTAC on the odds of lung cancer was shown in Supplementary Tables 2 and 3.

Discussion

This study showed that dTAC assessed either by FRAP or TRAP procedure is inversely associated with the odds of LC. The inverse association was observed in all LC subtypes. In addition, the inverse association was found in both men and women, water pipe users and non-users, opium users and non-users, and people less than 50 years old and over 50 years old. Furthermore, the odds of developing LC in smokers with higher antioxidant intake was almost half that of the lower intake group.

The importance of individual dietary antioxidants and the risk of LC has been studied extensively. Most studies showed that the higher intake of antioxidants such as β-carotene, α-carotene, β-cryptoxanthin, lycopene, and vitamin C reduce the risk of LC in nonsmokers [16, 30]. However, the results in female or male smokers are controversial [16, 30]. There is convincing evidence that high-dose β -carotene supplements in current and former smokers are associated with a higher risk of LC. Data on The differences between the association of natural food components with synthetic supplements raise the possibility that protective associations are not due to simple agents and there is an interaction between several antioxidants in the diet [31]. However, the actual effect of the total dietary antioxidant potential on the risk of LC has not been investigated. We believe that the TRAP and FRAP scores provide a better understanding of antioxidant intake and risk of cancer considering a more complete measurement of the counteracting factors in multifactorial cancer genesis pathways.

The main sources of antioxidants were grains, vegetables, and fruits in our population. Several studies have shown an inverse association between the consumption of grains, especially whole grains, and the risk of gastrointestinal and breast cancer [32, 33]. In some studies, consumption of vegetables and fruits was associated with a lower risk of LC; however, the evidence regarding the association between antioxidants and lung cancer (LC) risk remains inconclusive [34]. However, several studies, including systematic reviews, highlight the benefits of healthy dietary patterns such as the Mediterranean diet, the DASH diet, and the Healthy Eating Index in reducing LC risk [35, 36]. These dietary patterns emphasise the importance of a higher consumption of whole grains, fruits, and vegetables, which are rich in antioxidants [35, 36].

A systematic review examining the relationship between vegetable and fruit intake and LC risk revealed a nonlinear negative association. Specifically, risk reduction was observed up to 400 g/day of vegetables and 300 g/day of fruits [5]. The existence of this threshold effect underscores the importance of identifying optimal antioxidant intake levels. Current dietary guidelines recommend 2–3 servings of fruits and 3–5 servings of vegetables daily, which may provide sufficient antioxidants

Table 3 Risk of subtype of lung cancer according to tertiles of total antioxidant capacity (dTAC)scores in a large case/control study in Iran

			OR and 95% CI by tertile of dTAC intake				
			First tertile	Second tertile	Third tertile	P Trend	OR and 95%CI (continuous)
FRAP[3]		Control	1139	1136	1137	-	-
	Total	Case	250	192	174	-	-
		Model A[1]	Reference	0.77(0.63–0.95)	0.69(0.57–0.86)	0.001	0.80(0.72–0.89)
		Model B[2]	Reference	0.66(0.51–0.83)	0.53(0.40–0.68)	< 0.001	0.67(0.58–0.77)
	Small cell carcinoma	Case	44	28	32	-	-
		Model A[1]	Reference	0.64(0.39-1.0)	0.73(0.46–1.2)	0.16	0.82(0.64–1.1)
		Model B[2]	Reference	0.51(0.30–0.89)	0.55(0.32–0.96)	0.03	0.68(0.49–0.94)
	Adenocarcinoma	Case	82	77	74	-	-
		Model A	Reference	0.94(0.68–1.3)	0.90(0.65–1.3)	0.54	0.92(0.79–1.1)
		Model B	Reference	0.74(0.51–1.1)	0.61(0.41–0.9)	0.013	0.76(0.62–0.94)
	Squamous cell carcinoma	Case	74	58	39	-	-
		Model A	Reference	0.79(0.55–1.1)	0.53(0.36–0.78)	0.002	0.65(0.52–0.79)
		Model B	Reference	0.72(0.48–1.1)	0.45(0.28–0.73)	0.001	0.56(0.42–0.73)
	Other	Case	50	29	29	-	-
		Model A	Reference	0.58(0.38–0.93)	0.58(0.37–0.92)	0.016	0.78(0.61–0.99)
		Model B	Reference	0.51(0.29–0.84)	0.37(0.21–0.66)	0.009	0.64(0.48–0.88)
		Control	1139	1136	1137	-	-
	Total	Case	278	182	156	-	-
		Model A[1]	Reference	0.66(0.54–0.81)	0.56(0.45–0.69)	< 0.001	0.80(0.71–0.89)
		Model B[2]	Reference	0.54(0.42–0.68)	0.44(0.33–0.57)	< 0.001	0.71(0.61–0.83)
TRAP[4]	Small cell carcinoma	Case	51	30	23	-	-
		Model A	Reference	0.59(0.37–0.93)	0.45(0.27–0.74)	0.001	0.61(0.46–0.80)
		Model B	Reference	0.46(0.28–0.76)	0.35(0.19–0.62)	< 0.001	0.43(0.29–0.63)
	Adenocarcinoma	Case	95	72	66	-	-
		Model A	Reference	0.76(0.55-1.0)	0.69(0.50–0.96)	0.026	0.93(0.78–1.1)
		Model B	Reference	0.56(0.39–0.81)	0.49(0.34–0.74)	0.001	0.81(0.65–1.02)
	Squamous cell carcinoma	Case	84	49	38	-	-
		Model A	Reference	0.58(0.41–0.84)	0.45(0.31–0.67)	< 0.001	0.74(0.59–0.91)
		Model B	Reference	0.54(0.36–0.82)	0.45(0.28–0.72)	< 0.001	0.75(0.58–0.97)
	Other	Case	48	31	29	-	-
		Model A	Reference	0.65(0.41-1.0)	0.61(0.38–0.97)	0.03	0.78(0.60-1.0)
		Model B	Reference	0.53(0.32–0.89)	0.43(0.25–0.74)	0.002	0.66(0.48–0.92)

[1]Adjusted for energy (continues, Kcal/d), age(five categories), sex (female, male), and provinces(nine provinces of Iran)

[2]Further adjusted for SES (low, medium, high), opium use (never user, user), cigarette smoking (no, yes), water pipe use (no, yes), regular alcohol use (no, yes), workload physical activity (sedentary, moderate, heavy) and BMI (continues, kg/m^2)

[3]FRAP: Ferric Reducing Antioxidant Power of Diet

[4]TRAP: Total Radical-trapping Antioxidant Parameters of the diet

The association between different lung cancers with FRAP ($p=0.46$) and TARP ($p=0.11$) are not significantly different

There is no significant difference between the association of lung cancers with FRAP and TARP ($p=0.62$)

[37]. However, further research is needed to determine the effectiveness and safe dosage of antioxidant supplements.

Among all investigated non-dietary risk factors smoking, arsenic in drinking water, occupational exposures and indoor and outdoor air pollution have convincing evidence to be associated with LC. Smoking has the largest effect on LC incidence worldwide and smoking session is the main proposed strategy for LC control. However, smoking cessation is very difficult to achieve particularly in long-term abstinence. Most well-designed interventions showed little effect on the long-term abstinence rate [34, 35]. Therefore, investigating factors that decrease the risk of cancer or other smoking-induced diseases is of essential importance. Several studies have reported that the requirement for antioxidant vitamins increased in smokers due to oxidative stress induced by smoking [36–38]. Smokers have lower antioxidants, higher oxidative stress, and lower vitamin C and vitamin E status [39]. Consequently, an increased consumption of antioxidants has been suggested as a protective factor for smokers, although it may not entirely alleviate all the hazardous effects of smoking.

Our study showed that a higher dTAC score is associated with lower odds of LC in smokers. Several studies showed a reduction of some cancer or other chronic conditions by a higher intake of individual antioxidants in smokers [40]. However, no study investigates the association between dTAC scores and LC in smokers. Vegetable or fruit intake was associated with a lower risk of cancer in smokers, this association is usually stronger in smokers compared to nonsmokers. For example, A systematic review showed a 12 per cent reduction per 100 g/d vegetable intake in current smokers compared to 6% in the whole community. The corresponding figures are 8% compared to 9% for fruit intake [5]. The association between individual antioxidant intake and the risk of cancer may be different in smokers and non-smokers. However, evidence is insufficient to drive a firm conclusion at this time [5]. However, in our study, there is an inverse association between both smokers and non-smokers. All mentioned above, emphasize the importance of intake of an antioxidants-rich diet in smoker subjects as a risk-reducing strategy in these high-risk groups.

This is the first study that investigated the association between dTAC scores and the odds of LC in different subtypes of LC. The large sample size and the use of a validated FFQ are other strengths of our study. We carefully adjust our models for the most known risk factors of LC. Moreover, we evaluated the association in a stratified group of potential cofounders. The possibility of misclassification through assessing dietary intake by FFQ could not be rejected. However, this misclassification is non-differential and possibly could not affect the association between dietary scores and the risk of diseases. Moreover, the association between dTAC and odds of LC is too strong in our study which does not support the hypothesis of confounding as the sole explanation of the observed association.

This study has limitations related to its case-control design, mainly the recall bias. The second limitation is that the control group consisted of apparently healthy subjects who had not undergone pathological examinations like the cases. However, given that lung cancer is a serious and rapidly fatal disease in most patients, the inclusion of prevalent cases among the controls does not seem to be a significant issue. There are limitations related to dTAC scores. These scores do not consider all antioxidant activity of foods and mainly measure the in vivo antioxidant capacities of water-soluble ones [41]. However, the validity of dTAC scores (such as TRAP and FRAP) has been investigated previously in several settings. They showed high validity in food matrices [42, 43], animal tissue, and [43], human plasma [44] studies. Furthermore, there was a robust correlation between the consumption of foods rich in antioxidants and these scores, suggesting that they indeed provide an accurate assessment of antioxidant intake [44, 45]. A study in Sweden found a significant correlation between dietary dTAC estimated using FFQ and plasma TAC [46]. These scores were significantly correlated with healthier dietary patterns [47] and were associated with a lower risk of several other cancers [13, 48] and other chronic diseases in Iranian society [49, 50], therefore, it seems that dTAC scores are validated to be used in our study population.

Conclusion

high dietary antioxidant capacity was associated with lower odds of LC. The robust association observed across all subgroups underscores the significance of maintaining an antioxidant-rich diet for all individuals, including non-smokers with a lower risk of lung cancer.

Abbreviations

CI	Confidence Interval
dTAC	Dietary Total Antioxidant Capacity
FRAP	Ferric Reducing Antioxidant Power
FFQ	Food Frequency Questionnaire
LMICs	Low and Middle-Income Countries
LC	Lung Cancer
OR	Odds Ratio
SES	Social Economic Status
TRAP	Total Radical-trapping Antioxidant Parameters
WCF	World Cancer Fund

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-024-12914-2.

Supplementary Material 1

Author contributions

FT and KZ designed the research. MS and MH supervised primary data collection and cleaning. FT analyzed the data and performed the statistical analysis in consultation with BS, PB, and HR. FT wrote the draft. MG, MB, MM, and AR took part in designing the mother study and supervised data collections in different provinces. KZ was primarily responsible for the final content, and all authors reviewed and approved the final manuscripts.

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Data availability

Data of this study are available on a reasonable request by KZ.

Declarations

Ethical consideration

The ethics committee of Tehran University of Medical Sciences has approved this study (no. IR. TUMS.IKHC.REC.1400.314.). No data has been published with the names of the participants.

Consent for publication

It is not applicable because no data has been published on the names of the participants.

Competing interests

The authors declare no competing interests.

Consent to participate
All participants signed the informed consent after receiving a full description of the study. The ethics committee of Tehran University of Medical Sciences confirmed this study.

Statement of authorship
FT and KZ designed the research. MS and MH supervised primary data collection and cleaning. FT analyzed the data and performed the statistical analysis in consultation with BS, PB and HR. FT wrote the draft. MG, MB, MM, and AR took part in designing the mother study and supervised data collections in different provinces. KZ was primarily responsible for the final content, and all authors reviewed and approved the final manuscripts.

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