Mashhad University of Medical Sciences (MUMS)

Reviews in Clinical Medicine

Clinical Research Development Center Ghaem Hospital

The Mediterranean Diet and Lung Cancer; a Review of Case-Control Studies

Sepideh Hejazi (MD)[1], Sahar Ravanshad (MD)[2], Samaneh Sajjadi (MD)[2*]

[1]*Lung Diseases Research Center, Mashhad University of Medical Sciences, Mashhad. Iran.*
[2]*Department of internal medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.*

ARTICLE INFO

Article type
Review article

Article history
Received: 13 Mar 2021
Revised: 21 Apr 2021
Accepted: 24 Apr 2021

Keywords
Lung cancer
Mediterranean diet
Nutrition

ABSTRACT

Lung cancer is among the most common types of cancer with considerable mortality and morbidity around the globe. There are various risk factors involved in the development of lung cancer, and cancer prevention plans are mainly based on controlling the modifiable risk factors. While tobacco smoking is considered the main modifiable risk factor of lung cancer, some other modifiable factors including diet have become the center of attention in recent years. Although tobacco smoking control is one of the main strategies for preventing lung cancer in many countries, it has been discussed that eating a healthy diet can also be an adjuvant strategy for reducing the risk of developing lung cancer. In the present narrative review, we did a literature search for studies that addressed the effect of the Mediterranean diet on the development of lung cancer. Our findings show that different types of Mediterranean diets could be beneficial for reducing the risk of developing lung cancer.

Please cite this paper as:
Hejazi S, Ravanshad S, Sajjadi S. The Mediterranean Diet and Lung Cancer; a Review of Case-Control Studies. Rev Clin Med. 2021;8(1): 31-34.

Introduction

Cancers have a very high economic and clinical burden, and the risk of developing cancers for individuals under 74 years old is about 20% (1). Lung cancer is the most common cancer with more than 2 million new cases every year, also the leading cause of cancer-related deaths among males (1). Similar to other malignancies, lung cancer has both non-modifiable and modifiable risk factors. The non-modifiable risk factors of lung cancer are mainly genetic predisposition and a family history of lung cancer (2). The main modifiable risk factors include tobacco smoking, air pollution, and occupational exposures (2). Recently, consumption of specific foods and dietary behaviors have also been linked to the development of various types of cancer including lung cancer (3). It has been demonstrated that regular intake of vegetables and fruits, as well as aliments containing vitamins, selenium, antioxidants, and folic acid, prevents the development of common cancers including breast, colorectal, and lung cancer (4).

On the other hand, consumption of red meat and foods rich in animal fats has been linked to the development of lung cancer (5,6).

The combination of these good dietary habits is reflected in healthy diets such as the Mediterranean diet (5). It has been shown that the Mediterranean diet has beneficial effects on improving cardiovascular function and longevity

***Corresponding author:** Samaneh Sajjadi.*
Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
***E-mail:** sajjadis@mums.ac.ir*
***Tel:** 989151024463*

as well as cancer prevention (7,8).

This diet is based on the daily consumption of whole grains, fruits, vegetables, and olive oil, while consumption of animal proteins is reduced, mostly limited to fish and seafood (5). While the relationship between adhering to a Mediterranean diet and the development of various cancers has already been studied in the literature, there is not enough evidence summarizing the effect of the diet on the development of lung cancer.

Therefore, the present review study aimed to analyze the available evidence from case-control studies that evaluated the relationship between adhering to a Mediterranean diet and the development of lung cancer.

Literature review

The present narrative review was conducted doing a literature search on PubMed and Scopus online databases for all available case-control studies with the following keywords: ((("Lung Neoplasms"[Mesh]) OR ("lung neoplasm*"[TIAB]) OR ("pulmonary neoplasm"[TIAB]) OR ("bronchopulmonary neoplasm"[TIAB]) OR ("broncho-pulmonary neoplasm"[TIAB]) OR ("bronchial neoplasm"[TIAB]) OR ("lung cancer"[TIAB]) OR ("pulmonary cancer"[TIAB]) OR ("bronchopulmonary cancer"[TIAB]) OR ("broncho-pulmonary cancer"[TIAB]) OR ("bronchial cancer"[TIAB]) OR ("lung carcinoma"[TIAB]) OR ("pulmonary carcinoma"[TIAB]) OR ("bronchopulmonary carcinoma"[TIAB]) OR ("broncho-pulmonary carcinoma"[TIAB]) OR ("bronchial carcinoma"[TIAB]) OR ("bronchogenic carcinoma"[TIAB]) OR ("lung blastoma"[TIAB]) OR ("pulmonary blastoma"[TIAB]) OR ("bronchopulmonary blastoma"[TIAB]) OR ("broncho-pulmonary blastoma"[TIAB]) OR (bronchial blastoma[TIAB]) OR ("lung tumor"[TIAB]) OR ("pulmonary tumor"[TIAB]) OR ("bronchopulmonary tumor"[TIAB]) OR ("broncho-pulmonary tumor"[TIAB]) OR ("bronchial tumor"[TIAB])) AND ("Mediterranean").

Every English language article only focusing on the development of lung cancer was evaluated using the Newcastle-Ottawa Quality Assessment Form for Case-Control Studies. The findings are summarized in Table 1.

Table 1. Case–Control studies that evaluated the association between different types of Mediterranean diet and lung cancer

Author	Study duration (Years)	Location	Study population		Odds ratio or hazard ratio for lung cancer	Comments
			Case	Control		
Hawrysz et al. (9)	4	Poland	187	252	Smokers: The risk significantly reduced by 49% (OR: 0.51) in moderate and high adherence to the diet. Moderate smokers: The risk significantly lowered by 65% (OR: 0.35) for moderate and 66% (OR: 0.34) for high adherence to the diet.	The Polish version of the Mediterranean diet was associated with lower rate of lung cancer in smoker males.
Krusinska et al. (10)	-*	Poland	280	280	The risk significantly reduced by 51% (OR: 0.49) and 63% (OR: 0.37) when considering average and high adherence to the diet.	The Polish version of the Mediterranean diet was associated with lower rate of lung cancer.
Schulpen et al. (11)	20.3	Netherlands	2861	3720	The risk reduced non-significantly in men and women with hazard ratios of 0·91 and 0·73 respectively.	Higher adherence to the Mediterranean diet did not reduce the risk of lung cancer.
Hodge et al. (12)	17.8	Australia	403	34900	The risk significantly decreased by high adherence to the diet with a hazard ratio of 0.64.	Mediterranean diet is inversely associated with lung cancer.

Evaluating the diet within the previous year*

We found only four case-control studies that evaluated the relationship between adherence to different types of the Mediterranean diet and the development of lung cancer (9-12).

Two of these studies demonstrated that the Polish version of the Mediterranean diet was associated with a lower rate of lung cancer in general and in male smokers (9,10).

The Polish-adapted Mediterranean diet (Polish-aMED), including alcohol, was significantly

inversely associated with the risk of lung cancer among heavy smokers in Poland (9). Another study using the Polish-aMED excluding alcohol reported that moderate and high adherence to the diet was correlated with a reduced risk of lung cancer (10).

Based on the Hawrysz et al. study, the high and moderate adherence to the Polish-aMED reduces the risk of lung cancer by 49% in smokers (9).

The other two studies evaluated the Mediterranean diet (11,12). The study by Schulpen et al. in the Netherlands demonstrated that this type of diet is not correlated with the development of lung cancer (11). This study has the largest study population and the longest study period (11).

They also showed that adherence to a Mediterranean diet and development of lung cancer could be gender dependent, reporting that females with high adherence to the diet have a lower risk of developing lung cancer in contrast to males (11).

The Schulpen et al. study evaluating the alternate and modified Mediterranean diet scores did not include alcohol and reported that there was no significant relationship between adherence to the diet and development of lung cancer (11). Among these four studies, the relationship between adherence to the Mediterranean diet and the histopathological types of lung cancer has been studied only by Schulpen et al., and they reported that adherence to the Mediterranean diet may reduce the chance of developing adenocarcinoma and squamous cell carcinoma especially in males (11).

Mediterranean diet and prevention of lung cancer, possible links

The most recent systematic review and meta-analysis on the subject demonstrated that adherence to the Mediterranean diet is associated with a reduced risk of cancer mortality (13).

The Mediterranean diet has some unique features. First, this dietary regimen includes healthy fats, such as olive oil, as the main source of fats which have a considerable amount of omega-3 fatty acids (5). Considering fish as the preferred protein, taking dairy products and eggs, and limiting the consumption of red meat are the other healthy changes in the Mediterranean diet (5).

The primary beneficial effect of the Mediterranean diet on cancer development is mainly due to the antioxidants and anti-inflammatory properties of nuts, vegetables, and olive oil, as well as prohibiting the use of processed foods (14-16).

Fruits and vegetables are enriched with different vitamins, flavonoids, and folate which can prevent DNA damage (14,15). It has been shown that retinoids can inhibit tumorigenesis in the respiratory tract, and vitamin A intake is correlated with reduced lung cancer risk (17).

Although the Mediterranean diet does not have any considerable effect on the vitamin E level (18), a recent large-scale study with 28 years of follow-up indicated that higher vitamin E status is related to decreased risk of lung cancer (19).

Vitamin D is the other fat-soluble vitamin whose level increases by using a Mediterranean diet. Adherence to the Mediterranean diet has thus been linked to higher vitamin D levels, preventing osteoporosis (20). Moreover, a recent meta-analysis reported that there is an inverse relationship between vitamin D status and the development of lung cancer (21).

The omega-3 fatty acids of nuts and seafood present in the Mediterranean diet prohibit cancer development by affecting cellular proliferation (22). It has been demonstrated that omega-3 polyunsaturated fatty acids are immune-nutrients that play an important role in cell structure and signaling (22). Moreover, the omega-3 polyunsaturated fatty acids have anti-inflammatory potentials and modulate the pivotal pathways including apoptosis in lung cancer cells (22). On the other hand, the Mediterranean diet has a lower intake of fried or red meat which have been linked to the development of lung cancer (23).

It has been reported that high red meat consumption in heavy smokers not adhering to the Mediterranean diet is linked to an increased risk of lung cancer (24). Moreover, the Mediterranean diet replaces saturated or total fat, as a risk factor of lung cancer, with olive oil which is associated with lower cancer development risk (25).

A controversial component of the Mediterranean diet that is not strongly linked to the development of lung cancer is alcohol consumption. While some studies suggest that high alcohol consumption is a risk factor for lung cancer, others indicate that alcohol consumption in non-smokers cannot be a risk factor for cancer (26,27).

Conclusion

Although tobacco smoking control has been considered as one of the main strategies for preventing lung cancer in many countries, including Middle Eastern countries, it has been shown that sticking to a healthy diet can be an adjuvant strategy for reducing the risk of developing lung cancer.

One of the main limitations of the studies evaluating the effect of the Mediterranean diet on the development of lung cancer is the variable nature of this diet among different populations. The Mediterranean diet not only varies among the Mediterranean countries, but it is also diverse

within the same country (28). Different cultures, ethnicity, religions, and socioeconomic status affect the ingredients of a the Mediterranean diet (28). Therefore, the anticancer effect of the Mediterranean diet could vary among different populations.

Conflict of interest

All authors declare that they have no conflicts of interest.

References

1. Mattiuzzi C, Lippi G. Current Cancer Epidemiology. J Epidemiol Glob Health. 2019;9:217-222.
2. Malhotra J, Malvezzi M, Negri E, et al. Risk factors for lung cancer worldwide. Eur Respir J. 2016;48:889-902.
3. Malhotra J, Malvezzi M, Negri E, et al. Risk factors for lung cancer worldwide. Eur Respir J. 2016;48:889-902.
4. Donaldson MS. Nutrition and cancer: a review of the evidence for an anti-cancer diet. Nutr J. 2004;3:19.
5. Bach-Faig A, Berry EM, Lairon D, et al. Mediterranean diet pyramid today. Science and cultural updates. Public Health Nutr. 2011;14:2274-2284.
6. Martínez-González MA, Salas-Salvadó J, Estruch R, et al. Benefits of the Mediterranean diet: insights from the PREDIMED study. Prog Cardiovasc Dis. Jul-Aug 2015;58:50-60.
7. Mentella MC, Scaldaferri F, Ricci C, et al. Cancer and Mediterranean Diet: A Review.Nutrients. 2019;11:2059.
8. D'Innocenzo S, Biagi C, Lanari M. Obesity and the Mediterranean Diet: A Review of Evidence of the Role and Sustainability of the Mediterranean Diet. Nutrients. 2019;11:1306.
9. Mentella MC, Scaldaferri F, Ricci C, et al. Cancer and Mediterranean diet: a review. Nutrients. 2019;11:2059.
10. El-Sabban F. The antioxidant advantage of the Mediterranean diet in cardiovascular disease. Nutrition Dietary supplements. 2014;6:35-40.
11. Visioli F, Galli C. The role of antioxidants in the Mediterranean diet. Lipids. 2001;36 Suppl:S49-52.
12. Asadi Z, Ghaffarian Zirak R, et al. Dietary Inflammatory Index is associated with Healthy Eating Index, Alternative Healthy Eating Index, and dietary patterns among Iranian adults. J Clin Lab Anal. 2020;34:e23523.
13. Virtamo JJPotNS. Vitamins and lung cancer. Proc Nutr Soc. 1999;58:329-333. .
14. Castro-Quezada I, Román-Viñas B, Serra-Majem L. The Mediterranean diet and nutritional adequacy: a review. Nutrients. 2014;6:231-248.
15. Huang J, Weinstein SJ, Yu K,et al. A Prospective Study of Serum Vitamin E and 28-Year Risk of Lung Cancer. J Natl Cancer Inst. 2020;112:191-199.
16. Zupo R, Lampignano L, Lattanzio A, et al. Association between adherence to the Mediterranean Diet and circulating Vitamin D levels. Int J Food Sci Nutr. 2020;71:884-890.
17. Zhang L, Wang S, Che X,et al. Vitamin D and lung cancer risk: a comprehensive review and meta-analysis. Cell Physiol Biochem. 2015;36:299-305.
18. Vega OM, Abkenari S, Tong Z, et al. Omega-3 Polyunsaturated Fatty Acids and Lung Cancer: nutrition or Pharmacology? Nutr Cancer. 2021;73:541-561.
19. Sinha R, Kulldorff M, Curtin J,et al. Fried, well-done red meat and riskof lung cancer in women (United States). Cancer Causes Control. 1998;9:621-630.
20. Gnagnarella P, Maisonneuve P, Bellomi M, et al. Red meat, Mediterranean diet and lung cancer risk among heavy smokers in the COSMOS screening study. Ann Oncol. 2013;24:2606-2611.
21. Smith-Warner SA, Ritz J, Hunter DJ, et al. Dietary fat and risk of lung cancer in a pooled analysis of prospective studies. Cancer Epidemiol Biomarkers Prev. 2002;11:987-992.
22. Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and lung cancer risk in never smokers: a meta-analysis. Ann Oncol. 2011;22:2631-2639.
23. Freudenheim JL, Ritz J, Smith-Warner SA, et al. Alcohol consumption and risk of lung cancer: a pooled analysis of cohort studies. Am J Clin Nutr. 2005;82:657-667.
24. Maisonneuve P, Shivappa N, Hébert JR, et al. Dietary inflammatory index and risk of lung cancer and other respiratory conditions among heavy smokers in the COSMOS screening study. Eur J Nutr. 2016;55:1069-1079.
25. Morze J, Danielewicz A, Przybyłowicz K, et al. An updated systematic review and meta-analysis on adherence to mediterranean diet and risk of cancer. Eur J Nutr. 2021;60:1561-1586.
26. Bodén S, Myte R, Wennberg M, et al. The inflammatory potential of diet in determining cancer risk; A prospective investigation of two dietary pattern scores. PLoS One. 2019;14:e0214551.
27. Noah A, Truswell AS. There are many Mediterranean diets. Asia Pac J Clin Nutr. 2001;10:2-9.
28. Hawrysz I, Wadolowska L, Slowinska MA, et al. Adherence to Prudent and Mediterranean Dietary Patterns Is Inversely Associated with Lung Cancer in Moderate But Not Heavy Male Polish Smokers: A Case-Control Study. Nutrients. 2020;12:3788.
29. Krusinska B, Hawrysz I, Wadolowska L, et al. Associations of Mediterranean Diet and a Posteriori Derived Dietary Patterns with Breast and Lung Cancer Risk: A Case-Control Study. Nutrients. 2018;10:470.
30. Schulpen M, van den Brandt PA. Adherence to the Mediterranean diet and risk of lung cancer in the Netherlands Cohort Study. Br J Nutr. 2018;119:674-684.
31. Hodge AM, Bassett JK, Shivappa N, Hébert JR, English DR, Giles GG, et al. Dietary inflammatory index, Mediterranean diet score, and lung cancer: a prospective study. Cancer Causes Control. 2016;27:907-917.