# UW Integrative Health

Department of Family Medicine and Community Health



### **Lung Cancer Care and Prevention**

#### **Lung Cancer**

Lung cancer can originate from a variety of cell types within the lungs and is differentiated into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC accounts for 85% to 90% of lung cancers and includes squamous cell lung cancer, adenocarcinoma, and large cell carcinoma. SCLC grows more quickly and has often metastasized by the time of diagnosis.<sup>1</sup>

Lung cancer is the second most common cancer and the leading cause of cancer death in both men and women (25%). It is the most preventable cancer in the world.<sup>2</sup> Smoking is the primary cause of lung cancer while radon gas exposure is the second. Environmental carcinogen exposure to asbestos, arsenic, chromium, nickel, tar, mineral oils, mustard gas, silica, diesel exhaust, ionizing radiation, and bis(chloromethyl) ether also increase risk.<sup>3</sup>

Symptoms of lung cancer include a cough that is persistent or worsens, coughing up blood, shortness of breath or wheezing, chronic pneumonia or bronchitis, weight loss, and fatigue. Diagnosis is confirmed through history, X-ray, computerized tomography (CT), sputum, and biopsy. Lung cancer is primarily treated with surgery, and at times with chemotherapy and radiation depending on the type of tumor and extent of metastases.<sup>1</sup>

#### **Smoking**

Tobacco use accounts for 30% of all cancer deaths, causing 87% of lung cancer deaths in men and 70% of lung cancer deaths in women. Each year, over 7,000 nonsmoking adults die of lung cancer as a result of breathing secondhand smoke.<sup>2</sup> Squamous cell carcinoma and SCLC are most commonly associated with smoking. The risk declines with smoking cessation, reaching the risk level of nonsmokers after 20 to 25 years. The major lung carcinogens found in tobacco smoke are polycyclic aromatic hydrocarbons. Additionally, nicotine induces lung cancer cell line proliferation, promotes angiogenesis, and promotes resistance to apoptosis induced by chemotherapy.<sup>4</sup>

The United States Preventive Services Task Force (USPSTF) recommends annual lung cancer screening with a low-dose CT scan in adults aged 55 to 74 years who have a 30-pack per year smoking history and who currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Significant positive effects of smoking cessation on the health of lung cancer patients include decreased lung cancer risk, increased survival time, decreased postoperative complications, increased efficacy of chemotherapy, decreased radiation therapy complications, and improved quality of life. Immediate benefits of smoking cessation include improved oxygenation; lowered blood pressure; improved smell, taste, circulation, and breathing; increased energy; and

School of Medicine and Public Health UNIVERSITY OF WISCONSIN-MADISO

improved immunity. Lung cancer patients who quit smoking derive the same benefits plus decreased fatigue and shortness of breath; increased level of activity and performance; and improved appetite, sleep, and mood. This is especially important as lung cancer patients have a greater symptom burden than other cancer patients.<sup>4</sup>

See the "Nicotine Use Disorders" tool for more information on working with patients who smoke.

#### **NSAIDs and Aspirin**

The evidence for aspirin and nonsteroidal anti-inflammatory drug (NSAID) use to prevent lung cancer is mixed. A meta-analysis concluded that there was no relationship between aspirin use and lung cancer risk, since a significant protective effect was only seen in low-quality studies.<sup>5</sup> However, a larger meta-analysis concluded that aspirin use with a dose of seven tablets per week could significantly reduce lung cancer risk, but the beneficial effects were not seen in smokers.<sup>6</sup> At this time, it is not recommended to use aspirin or NSAIDs daily to prevent lung cancer, as the side effects may outweigh the benefits.

## Nonpharmacological Therapies for the Prevention and Treatment of Lung Cancer

#### **Nutrition**

#### Fruits and vegetables

A European prospective trial found that a 100-gm per day increase in the consumption of vegetables and fruits (about 1 to 2 servings) significantly reduced the risk of lung cancer, including in current smokers.<sup>7</sup> The intake of fruits and vegetables, especially those rich in carotenoids, reduces lung cancer risk.<sup>8-10</sup> Carotenoid-rich produce includes sweet potatoes, carrots, butternut squash, cantaloupe, sweet red peppers, apricots, peas, broccoli, spinach, and romaine lettuce.

#### Protein

Adequate protein intake is very important for patients with lung cancer since this type of cancer carries a high risk of cachexia. Their protein requirements can exceed 80 gm per day. The best dietary sources of protein are cold-water fish, legumes, lean meats (chicken and pork), nuts, and seeds.<sup>1</sup>

#### Soy

Soy foods consist of soybeans, tofu, tempeh, miso, and soymilk and are a common part of the Asian diet. A 2013 meta-analysis suggests a borderline reduction in lung cancer risk with daily soy protein intake, with a significant inverse association in nonsmokers.<sup>11</sup> The correlation is more apparent in women, with a significantly better overall survival.<sup>12,13</sup> These studies were conducted in Asian populations.

#### Obesity

Obesity is linked to the increased risk of many chronic diseases and cancers. However, being overweight or obese serves as a protective factor against lung cancer, especially in current and former smokers.<sup>14</sup> However, increased abdominal obesity may contribute to the development of lung cancer.<sup>15</sup> Decreased BMI from young adulthood to time of diagnosis is associated with worse outcomes in NSCLC and SCLC patients.<sup>16</sup> There is also significantly lower lung cancer-

School of Medicine and Public Health UNIVERSITY OF WISCONSIN-MADISON

related mortality in overweight and obese patients that transfers across sex, race, and smoking status.<sup>17,18</sup> Higher BMI is associated with a longer survival in lung cancer patients.<sup>19</sup> Weight loss should not be actively encouraged in overweight and obese patients with lung cancer, unless it will provide other health benefits.

#### **Dietary Supplements**

**Note**: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

#### **Beta-Carotene and Vitamin A**

Beta-carotene is a vitamin A precursor. The Alpha-Tocopherol Beta-Carotene Cancer Prevention (ATBC) trial and the Beta-Carotene and Retinol Efficacy Trial (CARET), found that supplemental beta-carotene increases the risk of cancer in current and former smokers.<sup>20,21</sup> However, higher dietary beta-carotene and vitamin A reduce the risk of lung cancer.<sup>22</sup>

The carcinogenic effect of beta-carotene stems from its ability to exacerbate DNA oxidative damage and modify p53-related pathways of cell proliferation and apoptosis, leading to the development of cancer. Long-term use of individual beta-carotene supplements was associated with elevated SCLC risk. The vitamins and lifestyle (VITAL) study concluded that a longer duration of retinol use was associated with a significantly higher risk of NSCLC and total lung cancer.<sup>23</sup> Smokers should be advised to avoid beta-carotene and vitamin A supplementation, but they may continue to increase the consumption of fruits and vegetables high in carotenoids.

#### **B** Vitamins, Homocysteine and Methionine

Higher levels of vitamin B6 and folate are associated with a reduction in lung cancer risk.<sup>24</sup> There is no association between vitamin B12 or methionine and lung cancer risk, but homocysteine may increase risk.<sup>25</sup> The intake of foods rich in B6, including cereal grains, legumes, vegetables, meat, fish, and eggs, is encouraged in current and former smokers.

#### Fish Oil

A randomized controlled trial (RCT) found that NSCLC patients taking 2.5 gm of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) per day during chemotherapy had a significantly increased response rate (35%) and a 40% greater clinical benefit.<sup>26</sup> Another RCT found that stage III NSCLC patients receiving two cans of a protein supplement containing 2.02 gm EPA and 0.92 gm DHA per day had significantly improved quality of life, physical and cognitive function, global health status, and social function after 5 weeks compared to the control group, which received only the protein supplement.<sup>27</sup> Fish oil has anti-inflammatory and antioxidative benefits and can be used to treat cachexia, a common problem in lung cancer patients.<sup>28</sup>

**Dose**: 1000-2000 mg of EPA + DHA daily. May cause bruising and increase risk of bleeding, consider avoiding if hemoglobin is less than 10 or platelets are less than 100.

#### Melatonin

Melatonin is a hormone secreted by the pineal gland that regulates the sleep cycle. Many studies have shown that lung cancer patients have disrupted melatonin secretion. Melatonin

School of Medicine and Public Health

prevents tumor metastasis in NSCLC via inducing apoptosis, inhibiting proliferation, invasion and metastasis, and enhancing of immunomodulation.<sup>29</sup> It also inhibits the progression of tumors due to its oncostatic, pro-oxidant and anti-inflammatory effects. Combining treatment with melatonin and chemotherapy maybe synergistic, contributing to prolonged survival and improved quality of life in patients with NSCLC.<sup>30</sup> A dose of 20 mg per day used by patients with metastatic NSCLC receiving chemotherapy results in a higher overall tumor regression rate and 5-year survival rate.<sup>31</sup> It can also be used in lower doses to help those experiencing insomnia.

**Dose:** The adjuvant dose of melatonin is 20 mg at night. For insomnia, the dose is 1 to 10 mg at night. The effective dose for sleep varies greatly from one person to another. Melatonin may cause excessive sedation, vivid dreams, and headaches.

#### **Physical Activity**

Preoperative exercise significantly improves pulmonary function before surgery, and reduces postoperative complication rate, length of stay, and improves quality of life in patients with lung cancer.<sup>32,33</sup> Four weeks of training is required preoperatively to obtain the aforementioned benefits, while 12 weeks of training is required if exercise is initiated postoperatively.<sup>34</sup> For patients with COPD, preoperative exercise training did not improve postoperative pulmonary complications, but it may result in faster recovery. <sup>35</sup> Encourage a regular exercise program preand postoperatively to improve outcomes in patients with lung cancer. In patients who do not exercise regularly, supervision with a trainer or enrollment into a pulmonary rehab program would be beneficial.

#### **Mind and Emotions**

#### **Breathing Exercises**

Breathing exercises in lung cancer patients function to correct breathing errors, reestablish a proper breathing pattern, increase diaphragm activity, improve alveolar ventilation, reduce energy consumption, and relieve shortness of breath. Simple breathing exercises consist of lengthening and slowing down inhalation and exhalation, allowing lung cancer patients to take deeper breaths that increase their oxygen intake, instead of shallow breaths that only utilize the top half of their lungs. Breathing exercises significantly improve postoperative pulmonary function, decrease the incidence of postoperative pulmonary complications, and reduce the length of hospital stay by over four days in patients with lung cancer. Both lung expansion techniques (pursed-lip breathing, sustained maximum expiration, breathing patterns, fractional inspiration and spirometry), as well as aerobic conditioning are effective.<sup>36</sup> There is also a significant improvement in quality of life, the performance of daily self-care and social activities, and symptoms of depression and anxiety.<sup>37</sup>

#### Reflexology

Reflexology involves applying pressure to the feet, hands, or ears with specific thumb, finger, and hand techniques without the use of oil or lotion. A Cochrane review of two small studies found that reflexology might have some short-lived benefits on anxiety and depression for lung cancer patients.<sup>38</sup>



#### Summary

Lung cancer is largely a preventable disease, and the first step is to assist patients with smoking cessation. Improvements in the diet to include fruits and vegetables can also reduce the risk of developing lung cancer, especially in smokers. Patients with lung cancer should be counseled on specific supplements, regular exercise, and breathing techniques that can improve their survival and quality of life. Lung cancer screening with a low-dose CT scan in adults aged 55 to 80 years who have a 30-pack per year smoking history and who currently smoke or have quit within the past 15 years is recommended by the USPSTF.

#### **Resource Links**

- <u>American Lung Association</u>: https://www.lung.org/support-community
- CancerCare®: http://www.lungcancer.org/
- Lung Cancer Alliance: http://www.lungcanceralliance.org/
- Lung Cancer Foundation of America: http://www.lcfamerica.org/
- Lung Cancer Research Foundation: http://www.freetobreathe.org/
- <u>Passport to Whole Health</u>: https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport\_to\_WholeHealth\_FY2020 508.pdf
- <u>Nicotine Use Disorders</u>: https://www.fammed.wisc.edu/files/webfmuploads/documents/outreach/im/tool-nicotine-use-disorder.pdf

#### Author(s)

"Lung Cancer Care and Its Prevention" was adapted for the University of Wisconsin Integrative Health Program from the original written by Srivani Sridhar, MD (2014, updated 2020). Modified for UW Integrative Health in 2021.

This Integrative Health tool was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

#### References

- 1. Alschuler LN, Gazella KA. The Definitive Guide to Cancer: An Integrative Approach to Prevention, Treatment, and Healing. 3rd ed. Celestial Arts; 2010.
- American Cancer Society. Key Statistics for Lung Cancer. American Cancer Society. Updated October 2019. Accessed April 2020, <u>https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html</u>
- 3. Najm W. Lung cancer. In: Rakel D, ed. Integr Med. 3rd ed. Saunders; 2012:704-709.
- 4. Cataldo JK, Dubey S, Prochaska JJ. Smoking cessation: an integral part of lung cancer treatment. Oncology. 2010;78(5-6):289-301.
- 5. Oh S-W, Myung S-K, Park J, Lee C, Kwon H. Aspirin use and risk for lung cancer: a meta-analysis. Ann Oncol. 2011;22(11):2456-2465.
- 6. Xu J, Yin Z, Gao W, et al. Meta-analysis on the association between nonsteroidal anti-inflammatory drug use and lung cancer risk. Clin Lung Cancer. 2012;13(1):44-51.
- 7. Büchner F, Bueno-de-Mesquita H, Linseisen J, et al. Fruits and vegetables consumption and the risk of histological subtypes of lung cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC). Cancer Causes & Control. 2010;21(3):357-371.

8. Wakai K, Matsuo K, Nagata C, et al. Lung cancer risk and consumption of vegetables and fruit: an evaluation based on a systematic review of epidemiological evidence from Japan. Jpn J Clin Oncol. 2011;41(5):693-708.

- Takata Y, Xiang Y-B, Yang G, et al. Intakes of fruits, vegetables, and related vitamins and lung cancer risk: results from the Shanghai Men's Health Study (2002-2009). Nutr Cancer. 2013;65(1):51-61.
- 10. Koutsokera A, Kiagia M, Saif MW, Souliotis K, Syrigos KN. Nutrition habits, physical activity, and lung cancer: an authoritative review. Clin Lung Cancer. 2013;14(4):342-350.
- 11. Wu SH, Liu Z. Soy food consumption and lung cancer risk: a meta-analysis using a common measure across studies. Nutr Cancer. 2013;65(5):625-632.
- 12. Yang W-S, Va P, Wong M-Y, Zhang H-L, Xiang Y-B. Soy intake is associated with lower lung cancer risk: results from a meta-analysis of epidemiologic studies. Am J Clin Nutr. 2011;94(6):1575-1583.
- 13. Yang G, Shu XO, Li HL, et al. Prediagnosis soy food consumption and lung cancer survival in women. J Clin Oncol. Apr 20 2013;31(12):1548-53. doi:10.1200/jco.2012.43.0942
- 14. Yang Y, Dong J, Sun K, et al. Obesity and incidence of lung cancer: a meta-analysis. International Journal of Cancer. 2013;132(5):1162-1169.
- Hidayat K, Du X, Chen G, Shi M, Shi B. Abdominal Obesity and Lung Cancer Risk: Systematic Review and Meta-Analysis of Prospective Studies. Nutrients. Dec 15 2016;8(12)doi:10.3390/nu8120810
- Shepshelovich D, Xu W, Lu L, et al. Body Mass Index (BMI), BMI change, and overall survival in patients with SCLC and NSCLC: a pooled analysis of the International Lung Cancer Consortium. J Thorac Oncol. Sep 2019;14(9):1594-1607. doi:10.1016/j.jtho.2019.05.031
- 17. Gupta A, Majumder K, Arora N, et al. Premorbid body mass index and mortality in patients with lung cancer: A systematic review and meta-analysis. Lung Cancer. Dec 2016;102:49-59. doi:10.1016/j.lungcan.2016.10.017
- 18. Zhu H, Zhang S. Body mass index and lung cancer risk in never smokers: a meta-analysis. BMC Cancer. Jun 5 2018;18(1):635. doi:10.1186/s12885-018-4543-y
- 19. Wang J, Xu H, Zhou S, et al. Body mass index and mortality in lung cancer patients: a systematic review and meta-analysis. Eur J Clin Nutr. Jan 2018;72(1):4-17. doi:10.1038/ejcn.2017.70
- 20. Heinonen OP, Albanes D. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med. 1994;330:1029-1035.
- 21. Omenn GS, Goodman GE, Thornquist MD, et al. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. N Engl J Med. 1996;334(18):1150-1155.
- 22. Yu N, Su X, Wang Z, Dai B, Kang J. Association of dietary vitamin A and β-carotene intake with the risk of lung cancer: a meta-analysis of 19 publications. Nutrients. Nov 11 2015;7(11):9309-24. doi:10.3390/nu7115463
- Satia JA, Littman A, Slatore CG, Galanko JA, White E. Long-term use of β-carotene, retinol, lycopene, and lutein supplements and lung cancer risk: Results from the vitamins and lifestyle (VITAL) study. Am J Epidemiol. 2009;169(7):815-828.
- 24. Johansson M, Relton C, Ueland PM, et al. Serum B vitamin levels and risk of lung cancer. JAMA. 2010;303(23):2377-2385.
- 25. Yang J, Li H, Deng H, Wang Z. Association of one-carbon metabolism-related vitamins (folate, B6, B12), homocysteine and methionine with the risk of lung cancer: systematic review and metaanalysis. Front Oncol. 2018;8:493. doi:10.3389/fonc.2018.00493
- 26. Murphy RA, Mourtzakis M, Chu QS, Baracos VE, Reiman T, Mazurak VC. Supplementation with fish oil increases first-line chemotherapy efficacy in patients with advanced nonsmall cell lung cancer. Cancer. 2011;117(16):3774-3780.
- 27. Van Der Meij B, Langius J, Spreeuwenberg M, et al. Oral nutritional supplements containing n-3 polyunsaturated fatty acids affect quality of life and functional status in lung cancer patients during multimodality treatment: an RCT. Eur J Clin Nutr. 2012;66(3):399-404.

School of Medicine and Public Health UNIVERSITY OF WISCONSIN-MADISO

School of Medicine and Public Health

- 28. Finocchiaro C, Segre O, Fadda M, et al. Effect of n-3 fatty acids on patients with advanced lung cancer: a double-blind, placebo-controlled study. Br J Nutr. 2012;108(02):327-333.
- 29. Ma Z, Yang Y, Fan C, et al. Melatonin as a potential anticarcinogen for non-small-cell lung cancer. Oncotarget. Jul 19 2016;7(29):46768-46784. doi:10.18632/oncotarget.8776
- Pourhanifeh MH, Sharifi M, Reiter RJ, Davoodabadi A, Asemi Z. Melatonin and non-small cell lung cancer: new insights into signaling pathways. Cancer Cell Int. 2019;19:131. doi:10.1186/s12935-019-0853-7
- Lissoni P, Chilelli M, Villa S, Cerizza L, Tancini G. Five years survival in metastatic non-small cell lung cancer patients treated with chemotherapy alone or chemotherapy and melatonin: a randomized trial. J Pineal Res. 2003;35(1):12-15.
- 32. Steffens D, Beckenkamp PR, Hancock M, Solomon M, Young J. Preoperative exercise halves the postoperative complication rate in patients with lung cancer: a systematic review of the effect of exercise on complications, length of stay and quality of life in patients with cancer. Br J Sports Med. Mar 2018;52(5):344. doi:10.1136/bjsports-2017-098032
- 33. Sebio Garcia R, Yáñez Brage MI, Giménez Moolhuyzen E, Granger CL, Denehy L. Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer: a systematic review and meta-analysis. Interact Cardiovasc Thorac Surg. Sep 2016;23(3):486-97. doi:10.1093/icvts/ivw152
- 34. Ni HJ, Pudasaini B, Yuan XT, Li HF, Shi L, Yuan P. Exercise training for patients pre- and postsurgically treated for non-small cell lung cancer: a systematic review and meta-analysis. Integr Cancer Ther. Mar 2017;16(1):63-73. doi:10.1177/1534735416645180
- 35. Li X, Li S, Yan S, et al. Impact of preoperative exercise therapy on surgical outcomes in lung cancer patients with or without COPD: a systematic review and meta-analysis. Cancer Manag Res. 2019;11:1765-1777. doi:10.2147/cmar.S186432
- Wang YQ, Liu X, Jia Y, Xie J. Impact of breathing exercises in subjects with lung cancer undergoing surgical resection: A systematic review and meta-analysis. J Clin Nurs. Mar 2019;28(5-6):717-732. doi:10.1111/jocn.14696
- 37. Liu W, Pan YL, Gao CX, Shang Z, Ning LJ, Liu X. Breathing exercises improve post-operative pulmonary function and quality of life in patients with lung cancer: A meta-analysis. Exp Ther Med. 2013;5(4):1194-1200.
- Rueda J, Solà I, Pascual A, Subirana Casacuberta M. Non-invasive interventions for improving wellbeing and quality of life in patients with lung cancer. Cochrane Database Syst Rev. 2011;(9):CD004282.