Dietary Influences on Lung Cancer: An Evaluation of the Research and Strategies to Help Counsel Patients
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When it comes to preventing lung cancer, many people think it's a simple prescription: Don't smoke. While there's no question that smoking is the most influential risk factor for developing lung cancer, there are several nutrition-related factors about which people should be informed.

Facing a lung cancer diagnosis is scary for patients and their families and friends. Often, rather than receiving hugs and support, lung cancer patients are shamed and stigmatized by a question that they may perceive as an accusation: "Did you smoke?"[1] But lung cancer is a complicated disease and ultimately results from a combination of environmental exposures and genetic risk factors.

RDs can help their healthy clients and patients reduce their risks of developing lung cancer, and medical nutrition therapy (MNT) plays an important role in helping to maintain a good quality of life for those diagnosed with the disease, both during treatment and beyond. Dietitians also play a key role in educating the public about risk factors for lung cancer and creating medical nutrition plans for those diagnosed with the disease.

Background and Epidemiology
Lung cancer is the second most common cancer diagnosis and the leading cause of cancer deaths worldwide.[2,3] Unfortunately, the overall five-year relative survival rate for those who are diagnosed with lung cancer is only 17%, compared with nearly 100% for prostate cancer and 89% for breast cancer.4 Mortality rates are highest among black men, followed by white men.[2,4]

The American Cancer Society estimates that in the United States in 2014, more than 224,000 people will be diagnosed with lung cancer, and more than 159,000 will die from the disease. Lung cancer takes more lives than breast, prostate, and colon cancers combined and accounts for 27% of all cancer deaths.[5]

Lung cancer forms in tissues of the lung, usually in the cells lining air passages. The two main types are small cell and non–small cell. The type of lung cancer is named for the size of the cancer cells when seen under a microscope. About 85% to 90% of lung cancers are non–small cell, while the remaining 10% to 15% are small cell.[6] It's rare for someone who has never smoked to have small-cell lung cancer.[6] The average age at the time of a lung cancer diagnosis is 70.[5]

According to the National Cancer Institute, a person is defined as a cancer survivor from the time of diagnosis forward, regardless of whether the person is considered cured.[7] In the United States, there are approximately 400,000 men and women living with a history of lung and bronchus cancer (183,410 men and 216,021 women).[8]

The National Lung Screening Trial has shown that screening current or former heavy smokers with low-dose CT scans can decrease their risk of dying from lung cancer. New screening guidelines adopted by the US Preventive Services Task Force plus increased awareness of who should be screened and how they can obtain their screening will be key for improving survival rates for those facing lung cancer.

Because of high incidence rates and low survival rates, it's important for RDs to understand and know how to address the risk factors that may cause lung cancer, ultimately trying to help patients prevent the disease.

It's been established that cigarette smoking is the most important risk factor for lung cancer. Although the possible association between physical activity and nutrition and the risk of lung cancer development remains controversial,[9] knowing about other modifiable risk factors may assist individuals in reducing their risk. The following information gives an overview of the current data.

Nonnutrition Risk Factors
Tobacco smoking causes about nine of every 10 cases of lung cancer in men and about eight of every 10 cases in women. People who smoke have about 20 times the risk of developing lung cancer than do people who don't smoke.[10]

In addition to smoking, risk factors for developing lung cancer include environmental exposures such as secondhand smoke, radon, asbestos, arsenic, nickel, and cadmium.[9,10]

Nutrition-Related Risk Factors
The following nutrition components have been studied and shown to potentially increase the risk of lung cancer:

Beta-Carotene and Antioxidants
Beta-carotene studies have garnered the greatest amount of news coverage in terms of lung cancer and nutrition research. Originally, increasing beta-carotene intake was thought to be one of the most promising ways to reduce lung cancer risk. However, the Carotene and Retinol Efficacy Trial found that beta-carotene, alone or in combination with vitamin E or retinyl palmitate (vitamin A), increased the incidence of lung cancer and cardiovascular disease mortality rates. It was one of the few nutrition and lung cancer trials involving humans; specifically, the study subjects were people exposed to asbestos in the workplace or who had a history of heavy smoking.

The study was stopped early because results showed an increase in lung cancer diagnoses and mortality among the group who received daily treatment consisting of a combination of 30 mg of beta-carotene and 25,000 IU of retinol in the form of retinyl palmitate.[11,12]

In addition, meta-analyses of primary and secondary cancer prevention trials examining dietary antioxidant supplements consistently have shown a lack of efficacy and an increased risk of lung cancer mortality involving beta-carotene.[13]

Phosphates

Recent genetic and dietary experiments in animal models have indicated that phosphates may be toxic to the body in various ways, including increasing the risk of cancer.

Dietary intake of phosphates has increased over the last several decades, as phosphates now are added to numerous processed foods, such as cheese, sausage, beverages, and baked goods. Researchers estimate that phosphate intake increased by 17% between 1983 and 1993.[14]

Phosphates are added to processed food products because they can increase food quality via improved water retention and texture. The FDA has given food phosphates Generally Recognized as Safe status, with no limits on their use. For the average American who consumes a diet based on fast and processed foods, phosphate intake is much higher compared with those whose diets are based on minimally processed foods.[14,15]

High phosphate load has been reported to cause cancer growth in animal models for both lung and skin cancer.[15] The only study conducted to date focusing specifically on phosphates and lung cancer involved mice. The findings showed a high dietary phosphate load (1%) resulted in increased oxidative stress and DNA damage, resulting in premature aging and shortened life span.[14]

The study results suggest that a high phosphate intake promotes tumorigenesis in lung cancer and may contribute to lung cancer development in individuals who are predisposed to the disease. This raises concerns for smokers or former smokers. The idea that excessive phosphate intake potentially could have a large public health impact is relatively new, therefore more studies will be needed to show that limiting phosphate intake could result in improved outcomes regarding lung cancer prevention.[15]

It's difficult to estimate a person's phosphate intake, as current nutrient databases may underestimate the phosphate content of foods.[16] According to the most recent USDA data (2010), Americans older than the age of 2 have an average daily phosphate intake of 1,386 mg. The Recommended Dietary Allowance is 1,250 mg for preteens and teenagers and 700 mg for adults, with a maximum tolerable level set at 4 g/day.

Many foods naturally contain phosphates, such as dairy and protein items, but not all of them are equally absorbed. Therefore, the amount of phosphates consumed doesn't always reflect levels in the blood. In addition, the body's phosphate requirements may vary according to age, sex, and daily activity. In addition, the presence of phosphorus-containing food additives may influence the amount of phosphates consumed as well.[17] RDs need to be cautious when advising clients because many factors influence phosphate metabolism.[18]

Since more research is needed, RDs should avoid making recommendations regarding phosphate intake and lung cancer risk. However, it's reasonable for RDs to advise clients to

focus on a diet consisting mostly of plant foods and limit their consumption of processed or fast foods, steps that contribute to keeping phosphate intake at healthful levels.

Nitrates/Nitrites
There's consensus that dietary nitrates essentially are inert and become biologically active only after being reduced to nitrites.

Vegetables are the primary dietary source of nitrates, and intake is determined by the type of vegetable consumed, the level of nitrates in the vegetables (including the nitrate content of fertilizer), the amount of vegetables consumed, and the level of nitrates in the water supply used to irrigate the crops.[19] Because the reduction of nitrates results in nitrite and other metabolic products, nitrates from vegetables can serve as a source of nitrites. Additionally, conventionally grown vegetables, compared with organic vegetables, may contain more nitrates as a result of the nitrogen-containing fertilizers used in the growing process.[20]

Although vegetables can serve as a source of nitrites, cured, processed meats actually are the primary source of nitrites in the average American diet. While nitrates are added to meats, they're subsequently converted to nitrite form to serve as antioxidants, develop flavor, and stabilize red color. Common meat products with added nitrates and nitrites include bacon, bologna, hot dogs, lunchmeats, sausages, and canned meat. The addition of nitrates and nitrites to meat must meet regulatory limits governed by the FDA and the USDA.[20]

Many of the meats to which nitrates are added are high in salt and nitrites, both of which are associated with an increased cancer risk. It's important to note that nitrates and nitrites aren't added to fresh, unprocessed meat.

Research consistently has shown a link between nitrite/nitrate intake and the risk of gastrointestinal cancer; the strongest data are for colorectal cancer. Therefore, the American Institute for Cancer Research's 2007 report ***Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*** recommends that people avoid processed meats.[21]

There's limited research on nitrates and nitrites with respect to lung cancer. In a 2012 case-control study, food-frequency questionnaires were used to collect dietary data about nutritional habits related to nitrates and nitrites (animal sources), and vitamin C and E intake from 80 Iranian adults (40 with lung cancer and 40 without) matched for sex and age. There was a positive association between animal sources of nitrates and nitrites intake and the risk of lung cancer.[22]

Acrylamide
Acrylamide is a probable human carcinogen present in commonly consumed carbohydrate-rich foods such as French fries and potato chips. According to a 2009 study, "Approximately 30% of calories consumed in the United States are from foods containing acrylamide."[23] While epidemiologic studies have shown that increased dietary acrylamide intake is associated with an increased risk of endometrial, ovarian, estrogen receptor–positive breast, and renal cell cancers, research on acrylamide and lung cancer remains in the early stages. A 2009 study in Dutch adults found differences in responses to acrylamide based on sex. The study findings showed there was no association in men, but there was an inverse association among women

who completed the study. The study authors concluded that "acrylamide may alter hormonal balances in such a way that it decreases lung cancer risk in women but increases endometrial and ovarian cancer risk."[24] It's clear that acrylamide plays a role in cancer development, but specifically regarding lung cancer risk, its role still needs to be determined.

B Vitamins

B vitamins and related enzymes are necessary for DNA replication, DNA repair, and gene expression regulation.

Two studies, both published in 2012, showed little evidence of an association between B vitamins or methionine and lung cancer risk. One study revealed that among current smokers, there was a reduced risk of lung cancer with higher intakes of riboflavin, although the association was weak.[25] The second study, involving women in China who had never smoked, found similar findings regarding riboflavin and lung cancer risk.[26]

The current findings regarding B vitamins and related enzymes remain inconsistent. Further investigation is needed to determine whether B vitamins influence lung cancer risk for smokers, former smokers, or nonsmokers.

Potentially Protective Foods

As mentioned previously, there's debate and conflicting evidence on nutrition-related risk factors for lung cancer. This debate is confounded by other lifestyle factors that influence risk. While there may be nutrients that reduce the risk of lung cancer, individuals' risks can be complicated by their smoking status.

In general, while specific nutrients are being investigated, human studies to date have shown the protective effects of certain nutrients in the context of foods. Consuming these nutrients in supplement form isn't recommended because research on their safety and efficacy is lacking.

A growing number of nutrients are being studied for their potential role in lung cancer prevention. Studies mostly are conducted on individual nutrients as opposed to larger food groups. However, a majority of studies have demonstrated an inverse association between the incidence of lung cancer and at least one food group: fruits and vegetables. But some studies have shown a clear protective effect only from fruit intake. It's unclear whether this inverse association is more pronounced in smokers or nonsmokers and whether some people have a genetic predisposition to respond more favorably to these foods.[9,22] Yong, lead author of a 1997 National Health and Nutrition Examination Survey follow-up study, concluded that "the daily consumption of a variety of plant foods, specifically fruits and vegetables, can provide a combination of nutrients and other potential protective factors to offer the best dietary protection against lung cancer."[27] Data since this study continue to support this conclusion.

Specifically for those with a high risk of lung cancer (those with a history of heavy smoking), significant risk reduction is found by adhering to a food intake pattern that's high in dietary fiber, potassium, vitamins C and E, total folate, and beta-carotene instead of diets that have an intake pattern high in animal products, starches, or polyunsaturated fatty acids.[28]

Tea

Tea has been studied for cancer prevention because of its antioxidant content. In general, the studies on tea and lung cancer risk have focused on flavonoids and indicate a small beneficial association, particularly among those who have never smoked.

A 2008 review of 12 studies on tea, flavonoids, and lung cancer revealed similar findings for green and black tea but became more significant when the most well-designed studies were considered. When tea intake and lung cancer were studied among never or former smokers, four of seven studies reported associations that were significantly protective.[29]

More recent studies done in China have confirmed the protective effects of tea on lung cancer risk, especially for nonsmokers. Drinking tea as little as three times per week produced positive benefits.[30,31]

Garlic

Garlic also has been known to have cancer-preventing properties, specifically for stomach and colorectal cancers. According to the American Institute for Cancer Research (AICR), there's preliminary data on the role that components of garlic may play in lung cancer prevention. These data come from laboratory studies showing diallyl disulfide has protective effects against several cancers, including lung cancer.[32]

The AICR also reports on studies in animal models that demonstrated slowed cancer development, including in the lungs, with increased intake of components of allium vegetables, of which garlic is a member.[32] However, studies specifically on garlic and lung cancer in humans are limited. Most recently, a 2013 study confirmed that human consumption of garlic may protect against lung cancer.[31]

Cruciferous Vegetables

Cruciferous vegetables have long been shown to have cancer-fighting properties. Epidemiologic evidence suggests that cruciferous vegetable intake may be weakly and inversely associated with lung cancer risk. The potential mechanism of action is the glutathione S-transferases function in metabolizing isothiocyanates. Therefore, variants in glutathione S-transferases genes have been shown to modify the association between cruciferous vegetable intake and lung cancer.[33]

A 2013 study suggested that, especially in women who have never smoked, the consumption of cruciferous vegetables may play a role in lung cancer risk reduction.[34]

Soyfoods/Isoflavones

Soyfoods have been studied for their cancer-protective effects for various cancers. A recent meta-analysis looked at studies of soy and soy isoflavones and concluded that "soyfood consumption may reduce lung cancer risk, particularly aggressive tumors, in nonsmoking women."[35] Another study, which was large and population based and took place in Japan, showed an inverse association between isoflavone intake and lung cancer risk in never-smokers.[36]

In addition to these encouraging findings on primary prevention, a 2013 study of lung cancer survivors showed that women who consumed soyfoods before their diagnosis had better overall survival rates.[37]

Carotenoids

As noted previously, findings from the Carotene and Retinol Efficacy Trial and similar trials have shown that beta-carotene supplementation increased, rather than decreased, lung cancer incidence. Because the results were unexpected, there have been several follow-up studies on the original participants as well as new studies to evaluate the connection between carotenoids and lung cancer risk. Researchers have found that the adverse effects persisted even after drug administration was stopped, although the effects no longer were statistically significant.[38]

A pooled analysis of seven cohort studies on lung cancer risk found that either no effect or a harmful effect was seen with supplemental beta-carotene. The effect was mostly equivalent, regardless of smoking status or the histological type of lung cancer.[39]

Findings from prospective cohort studies have suggested statistically insignificant inverse associations between dietary carotenoids and lung cancer. The researchers acknowledged that this may be a result of confounding factors, as the measurement of carotenoid intake may correlate with a more healthful diet.[40] In addition, specifically beta-cryptoxanthin intake (found in citrus fruits) slightly may lower the risk of lung cancer due to antioxidant function.[39]

Though beta-carotene supplements consistently have failed to provide benefits for those taking them, plant foods have demonstrated an important preventive influence in populations at high risk of lung cancer.[41] Scientists continue to try to identify how various carotenoids may be active in ways that would decrease lung cancer risk.[42,43] Food composition databases for specific carotenoids only recently have become available, so there's limited epidemiologic evidence relating usual dietary levels of these carotenoids with lung cancer risk.

Curcumin

Curcumin is a polyphenol that gives the spice turmeric its yellow color. It was first researched with respect to colorectal cancer prevention as part of in vitro laboratory studies followed by animal studies. Positive results led to a few small clinical trials in humans.

When it comes to lung cancer prevention, the data, all of which are from laboratory studies (both in vitro and in vivo), have shown that curcumin acts as a lung cancer preventative through its ability to assist a mutated cell with programmed cell death and stopping it from reproducing.[44-46] In addition, there's evidence that curcumin helps suppress inflammation.

Quercetin

Epidemiologic studies have shown that regular intake of foods high in quercetin is associated with a decrease in lung cancer diagnoses.[47] Quercetin, which can be found in foods and herbs such as citrus fruits, grapes, apples, onions, parsley, and sage, is the most abundant naturally occurring flavonoid.

Promising data show an inverse association between quercetin-rich foods and lung cancer risk. One study in particular identified a possible mechanism of quercetin-related changes in the expression of genes involved in metabolizing tobacco carcinogens in humans. This possible interplay among quercetin intake, tobacco smoking, and lung cancer risk is encouraging news, especially for current or former smokers.[47]

Vitamin D
Recent studies have looked at vitamin D intake and lung cancer risk, which, while still in preliminary stages of understanding, is important to address. Prospective cohort data from the Women's Health Initiative was published in 2013, and while they found no significant correlation overall, they did find an association between vitamin D and lowered lung cancer risk in postmenopausal women who never smoked.[48]

Results of a prospective study published in 2014 didn't show an association between vitamin D intake and any specific cancers, including lung cancer.[49] As with many of the other factors discussed in this article, RDs should avoid making recommendations regarding vitamin D intake and lung cancer risk until data prove conclusive.

MNT for Prevention and Survivorship
RDs can apply the research concerning diet and lung cancer to improve the lives of their patients and clients. They will benefit from counseling that discusses nutritional choices that may reduce their risk of developing lung cancer.

Dietitians also can provide MNT to help patients with lung cancer better tolerate treatment and reduce nutrition-related side effects; the patient handout "Coping With Nutrition-Related Consequences of Lung Cancer" is available for download at the end of this course.

Reducing Risk
"Observational studies of diet and lung cancer—both prospective and retrospective; in various countries; in smokers, ex-smokers, and never smokers; and for all histologic types of lung cancer—continue to strongly suggest that increased vegetable and fruit intake is associated with reduced risk in men and women."[50] This continues to be affirmed by current research findings. Smoking clearly is the most influential factor in reducing lung cancer risk. However, consuming a plant-based diet high in fruits and vegetables results in the optimal intake of nutrients known to reduce lung cancer risk.[27]

The following foods show promise for reducing the risk of lung cancer:

• tea (green, black, oolong, white);

• cruciferous vegetables (cabbage, broccoli, cauliflower, Brussels sprouts, kale, bok choy);

• soyfoods (soybeans, tempeh, tofu, soymilk, soy nuts, edamame, miso soup);

• carotenoid-rich foods (carrots, sweet potatoes, dark-green leafy vegetables, tomatoes);

• curcumin (found in mustard, turmeric, or curry); and

• quercetin (found in citrus fruits, apples, onions, parsley, sage, tea, olive oil, grapes, dark cherries, dark berries).

While nothing magical occurs if you include these foods in a diet full of processed foods, the biggest impact will come when these foods are included in the context of a plant-based diet. Advising your clients and patients to consume these foods at least three times per week would be a good place to start.

MNT for Lung Cancer Patients
Research has shown that nutrition intervention by RDs for patients receiving intensive chemotherapy for small-cell lung cancer resulted in improved weight status and quality of life.[51]

Nutrition-Related Side Effects
Lung cancer patients can face various nutrition-related side effects depending on what type of treatment they receive and the part of the lung toward which treatment is directed. Radiation treatment to part of the lung closest to the esophagus, for example, increases the possibility of developing esophagitis.

Some of the most common nutrition-related side effects of cancer and its treatments are poor appetite, weight loss, fatigue, and muscle turnover. Depending on the stage and severity of their diagnoses, patients may be diagnosed with cancer cachexia, a chronic loss of skeletal muscle mass that results in progressive functional impairment.[52] For those with intense chemotherapy and concurrent radiation, dehydration also is a risk. Nutrition-related side effects can be minimized through close monitoring of these patients' weight and nutritional intake.

In determining calorie needs, the Academy of Nutrition and Dietetics' Evidence Analysis Library calls for using measured resting energy exchange. However, it also notes that if it isn't possible or imperative to measure resting energy exchange, the Harris-Benedict equation should be used to estimate calorie needs. Some evidence indicates that this equation may underestimate energy needs by an average of 12% to 13%, though. Fortunately, most cancer patients in active treatment are weighed at least once per week, so it's relatively easy to adjust calorie recommendations based on their weight.[53]

Among patients with advanced non–small-cell lung cancer who are undergoing chemotherapy, information in the Evidence Analysis Library doesn't recommend consuming antioxidants (vitamins C and E, beta-carotene, selenium) above the Tolerable Upper Intake Level in order to improve treatment outcomes. It also reports that, for this population, "using multiple high-dose oral antioxidants didn't significantly influence response to treatment, survival, survival time, and chemotherapy toxicity."[54]

Making a Difference
There's hope for preventing lung cancer and improving the survival of individuals afflicted with this disease. In addition to applying your training as an RD to help individuals with lung cancer, the way you communicate also can make a difference. For example, the next time you meet someone who has been diagnosed with lung cancer, resist the inadvertent tendency to blame or stigmatize patients by asking whether they are or were smokers.[1] Instead, ask how you can help them with any nutrition-related side effects of treatment. You also can honor them by knowing their cancer ribbon color (clear or white) and celebrating Lung Cancer Awareness Month (November). Your concern will stand out and make a difference.

—Julie Lanford, MPH, RDN, CSO, LDN, serves as the wellness director for Cancer Services in Winston-Salem, North Carolina. She coordinates survivorship and prevention programs and also writes the organization's prevention and survivorship blog at CancerDietitian.com.

Click here for the patient handout "Coping With Nutrition-Related Consequences of Lung Cancer."

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54. What evidence suggests a relationship between supplementation of multiple antioxidants and an interaction with paclitaxel and carboplatin chemotherapy protocols and tolerance of chemotherapy treatment in patients with non-small cell lung cancer? Academy of Nutrition and Dietetics Evidence Analysis Library website. http://andevidencelibrary.com/template.cfm?template=guide_summary&key=1836. Accessed March 6, 2014.

Examination

1. When a patient with lung cancer reports poor appetite and weight loss, which of the following should an RD do to address the problem?
A. Prescribe nutritional supplements.
B. Recommend an appetite stimulant.
C. Estimate calorie needs, monitor weight weekly, and adjust calorie recommendations based on the patient's weight.
D. Intervene only after weight loss has exceeded 10% of usual body weight.

2. Current evidence suggests that antioxidants in supplement form reduce the risk of lung cancer, especially among high-risk individuals.
A. True
B. False

3. What is the overall five-year survival rate for people diagnosed with lung cancer?
A. 17%
B. 54%
C. 89%
D. 100%

4. Lung cancer takes more lives than breast, prostate, and colon cancers combined.
A. True
B. False

5. What is one common nutrition-related side effect that lung cancer patients face?
A. Weight gain
B. Poor appetite
C. Thick saliva
D. Bloating

6. Which of the following food items or additives does current research suggest shows promise for reducing the risk of lung cancer?
A. Coconut oil
B. Plant sterols
C. Gluten
D. Soyfoods

7. What nutrition component discussed in this course may alter hormonal balances in such a way that it decreases lung cancer risk in women but increases endometrial and ovarian cancer risk?
A. Gluten
B. Aspartame
C. Acrylamide
D. Soy

8. Specifically for those at high risk of lung cancer, significant risk reduction is found with adherence to a food intake pattern that includes which of the following?
A. Dietary fiber
B. Animal products
C. Starch
D. Polyunsaturated fatty acids

9. Which of the following meals includes more of the food items or additives shown by research to decrease the risk of lung cancer?
A. Chicken enchilada with tortilla chips and salsa
B. Sausage and onion quiche with melon
C. Cold-cut sandwich, baked potato chips, and a banana
D. Curried lentils with kale and a baked sweet potato

10. Based on the current evidence, switching from a processed beverage to a brewed green tea would potentially decrease the risk of lung cancer.
A. True
B. False