Alcohol as a Risk Factor for Cancer

Yin Cao and Edward L. Giovannucci

Objective: *To summarize epidemiologic evidence of alcohol as a risk factor for many types of cancers and discuss available resources to help patients reduce alcohol intake.*

Data Sources: *Published epidemiologic literature and resources available for alcohol reduction.*

Conclusion: *Heavy alcohol intake has been linked to increased risk of several cancers, including cancer of the colon, rectum, female breast, oral cavity, pharynx, larynx, liver, and esophagus; whereas light-to-moderate drinking (up to one drink per day for women and up to two drinks per day for men) is not appreciably associated with cancer risk and may be beneficial for cardiovascular disease. Among the healthy population and cancer survivors, those already drinking in moderation may continue to do so. Interactive tools can be used to track drinking and set goals for reducing alcohol intake. Medications and social support are available for alcoholics.*

Implications for Nursing Practice: *Nurses may utilize epidemiologic evidence and resources available to educate patients about their cancer risk associated with alcohol intake and provide support for reducing intake.*

Key Words: *alcohol, standard drink, light-to-moderate drinking, alcoholism, cancer, cancer survival.*

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Alcohol is commonly consumed in our society. In the United States, 87.6% of people 18 years of age and older reported that they drank alcohol at some point in their lifetime and 71.9% reported that they drank in the past year.[1] The fact that the use of alcohol is so visible and accepted globally has overshadowed the fact that alcohol contributes to many health and social problems. It is estimated that 3.6% of all cancers worldwide (1.7% in women, 5.2% in men) were attributable to alcohol consumption,[2] and 3.2% to 3.7% of cancer deaths in the United States,[3] primarily based on relative risks from studies focused on high intake of alcohol.

Descriptive Epidemiology of Alcohol as a Cancer Risk Factor

In the United States, *one standard drink* contains roughly 14 grams of pure alcohol, which is found in 12 ounces of regular beer, 5 ounces of wine, or 1.5 ounces of distilled spirits. Heavy alcohol consumption, commonly defined as more than one drink per day for women and more than 2 drinks per day for men, has been linked to an increased risk of several cancers, including cancer of the colon, rectum, female breast, oral cavity, pharynx, larynx, liver, and esophagus.[4] These eight cancers were considered as causally related to alcohol consumption according to the International Agency for Research on Cancer, and ethanol in alcoholic beverages was classified as "carcinogenic to humans." The dose-response relationship varies by cancer site, with the highest relative risk for the upper aerodigestive tract, including cancers of the oral cavity, pharynx, larynx, and esophagus. The relative risks associated with alcohol consumption are less for colorectal and breast cancer but the absolute number of cases attributable to these cancers is high.[5] Overall, the total amount of alcohol consumed over time, not the type of alcoholic beverage, seems to be the most important factor cancer risk. High intake of alcohol may also be associated with an increased risk of stomach,[6] pancreas,[7] and lung cancer.[8,9]

According to the Dietary Guidelines for Americans,[10] *light-to-moderate drinking* is defined as up to 1 drink per day for women and up to 2 drinks per day for men and is more prevalent than heavy alcohol consumption in the United States; about 46% of adults are light-to-moderate drinkers, and 5.4% are heavy drinkers. Extensive literature has documented the J-shaped associations between alcohol intake and a variety of diseases, including multiple cardiovascular outcomes[11] such as congestive heart failure and[12,13] stroke,[14] as well as diabetes[15] and possibly coronary heart disease,[16] whereby light-to-moderate drinkers have less risk than abstainers, and heavy drinkers are at the highest risk. Thus, the potential benefits of light-to-moderate alcohol consumption have to be weighed against the other possible health risks, and cancer is a major concern. However, the association between light-to-moderate drinking with cancer and the above alcohol-related cancers is less clear.[17,18]

In a recent analysis of two large prospective US cohort studies, the Nurses' Health Study and the Health Professionals Follow-Up Study, we quantified risk of cancer across all levels of alcohol consumption among women and men separately, with a focus on light-to-moderate drinking and never smokers.[19] Overall, light-to-moderate drinking (<15 g/d for women and <30g/d for men) was associated with a small but non-significant increased risk of cancer in both women and men, consistent with findings from women in the British Million Women study.[17] For men, the association with alcohol-related cancers (cancer of the colorectum, oral cavity, pharynx, larynx, liver, and esophagus[4]) was observed largely in alcohol drinkers who also smoked, and moderate drinking did not appreciably increase risk in never smokers. Among women, even a consumption of 5 to 14.9 g/d was associated with increased risk of alcohol-related cancers, mainly breast cancer.

Heavy episodic or binge drinking is not consistently defined across studies, but one commonly used definition in the United States, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), is four or more drinks at one time for a woman and five or more drinks at one time for a man, resulting in a person's blood alcohol concentration to 0.08 g/dL. One in six US adults binge drink about four times a month, consuming about eight drinks per binge episode. While binge drinking is more common among young adults aged 18 to 34 years, binge drinkers aged 65 years and older report binge drinking more often (an average of five to six times a month).[20] Binge drinking was associated with an increased risk of breast cancer compared with women who consumed the same amount of total alcohol but did not binge drink.[21]

Among cancer survivors, the prevalence of alcohol use generally mirrors that of the general population, although it is higher among some patients (eg, prostate and head and neck cancers).[22] Findings from studies on alcohol and cancer recurrence and survival among cancer patients have not been consistent and have varied by cancer sites.[23-26] For head and neck cancers, continued alcohol consumption is associated with lower survival rates.[25] However, findings for breast cancer are mixed. A recent study of 23,000 breast cancer patients found that alcohol intake before and after diagnosis was not associated with breast cancer-specific survival, and one possible explanation was that the kind of breast cancer that is more likely to be diagnosed among women who drink may be more responsive to hormone-modifying therapies and is less fatal. However, women consuming moderate levels of alcohol, either before or after diagnosis, experienced better cardiovascular and overall survival than nondrinkers.[26]

Pathophysiological Mechanisms Underlying Risk Factor

Acetaldehyde, the first and most toxic ethanol metabolite, is considered to be a cancer-causing agent.[27] Acetaldehyde promotes cancer development through multiple mechanisms, including interference with DNA replication, induction of DNA damage, and formation of DNA adducts.[28] Alcohol dehydrogenase (ADH) enzymes oxidize ethanol to acetaldehyde, and aldehyde dehydrogenase (ALDH) enzymes oxidize the acetaldehyde to the non-toxic acetate. People who carry *ADH* (alcohol dehydrogenase) alleles that encode ADH enzymes with high activity or *ALDH* alleles that encode ALDH enzymes with particularly low activity are at increased risk of alcohol-related cancers.[29,30] Low active ALDH enzymes are especially prevalent in individuals of East Asian descent. Ethanol may also stimulate carcinogenesis by inhibiting DNA methylation and interacting with retinoid metabolism.

The specific mechanisms linking alcohol and risk of a particular cancer type may vary. Bacterial microbiota contributes to the metabolism of alcohol and may mediate many of the disease-promoting and genotoxic effects of alcohol,[31] particularly for colorectal cancer,[32] as well as cancers of the oral cavity, where saliva acetaldehyde were found to be high for increasing ethanol intake and further metabolism of acetaldehyde is limited.[33]

In addition, synergistic effects of alcohol and smoking were observed for cancers of the upper aerodigestive tract.[19,34,35] Smokers have twice as much acetaldehyde in their saliva as nonsmokers if they consume the same amounts of alcohol.[36] Cigarette smoke itself has large amounts of acetaldehyde that dissolves in the saliva during smoking, and smoking may also increase the capacity of oral yeasts and bacteria to produce more acetaldehyde from ethanol.[28,37] In addition, carcinogenic mechanisms associated with alcohol and smoking may differ but interact to increase risk; for example, alcohol may increase tissue susceptibility to carcinogens from tobacco by increasing the permeability of tobacco-specific carcinogens,[38] or the induction of cytochrome P450-2E1(CYP2E1) in mucosa of the upper aerodigestive tract to enhance activation of procarcinogens in tobacco, such as polycyclic hydrocarbons and various nitrosamines.[39]

For breast cancer, cell line studies suggested the following mechanisms may be involved in the link between alcohol and breast carcinogenesis: increased hormonal receptor levels, increased cell proliferation, a direct stimulatory effect, DNA adduct formation, increase cyclic adenosine monophosphate, change in potassium channels and modulation of gene expression. Alterations in blood hormone levels, especially elevated estrogen-related hormones, have been reported in humans.[25,40] Human studies have also suggested a connection with prolactin and with biomarkers of oxidative stress.

Evidence-Based Strategies to Reduce Risk: Public Policy, Professional and Public Education Initiatives/Clinical Interventions

For the general population, the 2015–2020 *Dietary Guidelines for Americans*[10] recommends that if alcohol is consumed, it should be in moderation (up to one drink per day for women and up to two drinks per day for men), and only by adults of legal drinking age. The Guidelines also **do not** recommend that individuals who do not drink alcohol start drinking for any reason.

It is important for oncology nurses to be aware of the resources available to help individuals reduce their alcohol intake. Table 1 provides a list

TABLE 1.
Resources Available for Alcohol Assessment, Reduction and Treatment

Purpose	Link	Suggestions
Assessment of alcohol intake	http://rethinkingdrinking.niaaa.nih.gov/	Interactive tools for assessing and changing risky drinking; a 16-page booklet can be ordered online for patient education
	DrinkControl, AlcoDroid Alcohol Tracker, etc.	Mobile apps for tracking alcohol intake to adhere to moderate drinking guidelines
Reduction in the general population	http://rethinkingdrinking.niaaa.nih.gov/Thinking-about-a-change/Strategies-for-cutting-down/Tips-To-Try.aspx	Include tips for reducing intake from the NIAAA (301-443-3860); Substance Abuse and Mental Health Services Administration also provides 24-hour Help Hotline: 800-662-4357
Specialty treatment of alcoholism	http://rethinkingdrinking.niaaa.nih.gov/Help-links/Default.aspx#Professional	Contact the primary care doctor, health insurance company, local health department, or employee assistance program, or the Treatment Facility Locator (800-662-4357), or check the link for medical or non-medical addiction specialists
Mutual support groups	http://rethinkingdrinking.niaaa.nih.gov/Help-links/Default.aspx#Professional	Include resources for mutual support; for example, Alcoholics Anonymous (AA) 212-870-3400 and Al-Anon Family Groups: 888-425-2666.

Abbreviation: NIAAA, National Institute on Alcohol Abuse and Alcoholism.

of resources for alcohol assessment, reduction, and treatment.

The NIAAA provides the following tips for cutting down alcohol intake (http://rethinkingdrinking.niaaa.nih.gov/Thinking-about-a-change/Strategies-for-cutting-down/Tips-To-Try.aspx):

- keep track of how much you drink
- count and measure drinks accurately
- set goals on how many days a week and how many drinks you will have on those days
- pace yourself and have no more than one standard drink in an hour
- do not drink on an empty stomach
- find alternatives and fill free time by developing new, healthy activities, hobbies, and relationships, or renewing ones you've missed
- avoid "triggers"
- plan to handle urges by reminding yourself of your reasons for changing or talk things through with someone you trust
- know your "no": if offered a drink at times when you don't want one. Have a polite, convincing "no, thanks" ready

For individuals dependent on alcohol, in addition to the tips above, social support is important, including: 1) educate family and friends, 2) develop new interests and social groups, 3) find rewarding ways to spend your time that don't involve alcohol, and 4) ask for help from others. When asking for support, be specific on how others could help, for example, 1) not offering you alcohol, 2) not using alcohol around you, 3) giving words of support and withholding criticism, 4) not asking you to take on new demands right now, 5) attending a mutual support group like Alcoholics Anonymous (refer to http://rethinkingdrinking.niaaa.nih.gov/Help-links/Default.aspx#Professional for mutual support groups for both individuals and family with affected individuals).

Treatment either through medications or behavioral therapy is available. Primary care and mental health practitioners can provide effective alcoholism treatment by combining new medications with a series of brief counseling visits. A clinician's guide can be found at http://www.niaaa.nih.gov/guide. For specialty addiction treatment options, please refer to http://rethinkingdrinking.niaaa.nih.gov/Help-links/Default.aspx#Professional.

For patient education, the Web site built by the NIAAA provides interactive tools for assessing and changing risky drinking (http://rethinkingdrinking.niaaa.nih.gov/). A 16-page booklet "Rethinking drinking" describes risky drinking patterns and symptoms of a problem, and provides support and resources for making a change, and can be ordered online for patient education for free (http://pubs.niaaa.nih.gov/publications/RethinkingDrinking/OrderPage.htm). Other easy-to-read materials for the public that cover a wide range of

alcohol-related topics can be found at http://www.niaaa.nih.gov/publications/brochures-and-fact-sheets.

Evidence is accumulating addressing the optimal balances of risks and benefits of alcohol intake among patients with cancer. Nonetheless, at present, guidelines for cancer survivors from major organizations, including the American Institute for Cancer Research, American Cancer Society, American Society for Clinical Oncology,[41] suggest that women should limit alcohol intake to no more than 1 drink per day, and men should limit alcohol intake to no more than 2 drinks per day, which is consistent with guidelines for the general population. Additionally, health care providers should tailor advice on alcohol consumption to the individual cancer survivor, according to cancer type and stage of disease, treatment, treatment-related side effects, risk factors for recurrence or new primary cancers, and comorbid conditions.[42] Many health care professionals ask individuals receiving chemotherapy or biological therapy to avoid alcohol consumption during treatment. For instance, procarbazine, commonly used to treat Hodgkin's disease, and lomustine, used for brain tumors, can interact with alcohol, causing sickness, headaches, difficulty breathing, sweating, faintness, or drowsiness. Limited alcohol intake is also suggested for patients with mucositis and among those beginning head and neck radiation therapy or chemotherapeutic regimens that put them at risk for mucositis.

Genetic predisposition is another factor that must be taken into account when discussed individually on the most appropriate levels of drinking. Skin flushing after consumption of alcohol is typically related to low active *ALDH* genotypes that allow increased acetaldehyde levels after alcohol consumption, especially in East Asian individuals. Some evidence suggests that the tendency to flush accentuates the effect of alcohol consumption on risk of cancer.[43] Although genetic testing of *ADH* and *ALDH* alleles is less likely to be offered in the healthy population or cancer survivors, a family history of cancer may provide extra information regarding future risk of cancer. We[44] and others[45,46] observed a stronger association of alcohol intake and risk of colorectal cancer among people who had a family history of colorectal cancer; however, minimal differences were observed among people with versus without a family history of breast cancer in their risk of breast cancer.[19] More research is warranted to confirm these findings. Health professionals should emphasize the importance of limited alcohol intake to patients with a family history of colorectal and breast cancer because absolute risk of these cancers is much higher among these individuals compared with people without a family history, and limited alcohol intake may help reduce such risk.

Apps, Social Media, Other Communication Strategies That Might be Useful

Apps

Many mobile apps have been developed to either help light-to-moderate drinkers not to go beyond recommended guidelines, or closely monitor consumption among people who are addicted to alcohol, provide assistance in case of overuse, and provide support to stop drinking. For example, *DrinkControl* is a mobile app for iPhone and Android phones that allows tracking and converting of daily alcohol intake quantities, such as glasses, bottles, or cans, into the standard units of alcohol, and alerts people when they are exceeding the limits set by moderate drinking guidelines, as well as how much money they have spent on drinks and consumed alcohol calories. It also lets one compare day-to-day drinking tendencies with the moderate drinking guidelines of the leading international health organizations. In addition to keeping a record of the number of drinks, *AlcoDroid Alcohol Tracker* allows one to set a goal to see how well he or she is doing. An in-app blood alcohol calculator also gives a reading if one is intoxicated. To ensure accountability, drinking episodes can be shared via social apps or e-mail for others to see. The best alcoholism iphone and Android apps of 2015 can be found at http://www.healthline.com/health/addiction/top-alcoholism-iphone-android-apps#2.

Social Media

Social media have a broad reach into the lives of many young people and have created a new environment in which adolescents and young adults may be exposed to and influenced by alcohol-related content. Although we have primarily focused on adult alcohol intake and risk of cancer in this article, the impact of early life drinking on later risk of diseases cannot be overemphasized,[21,47] and as such the importance of social media should not be ignored. Social media can provide information on individual consumption[48] or may serve as a source of influence on behavior.[49] Although exposure to traditional media and commercial communications on alcohol is associated with the likelihood

of starting drinking among adolescents, the influence of alcohol advertising in social media remains to be understood and efforts to use social media for prevention or interventions for alcohol abuse have just started.[50]

Conclusion

Alcohol is a complex behavior in our society. The impact of alcohol on cancer risk is just one of the concerns, albeit an important one, in regards to the overall health and social aspects of alcohol consumption. Light-to-moderate drinking, defined as up to one drink per day for women and up to two drinks per day for men, is not appreciably associated with cancer risk, and may be beneficial for cardiovascular disease and overall mortality. Although it is generally not advisable for abstainers to begin alcohol drinking for health benefits, it is reasonable for those already drinking at moderate levels, including cancer survivors, to continue to do so if they wish. Nonetheless, some subgroups, especially those with a family history of colorectal cancer, possibly breast cancer, or who experience facial flushing after alcohol consumption, may be at increased risk for some cancers if they consume alcohol. Those who drink at levels beyond those defined as light-to moderate are at higher risk of cancer, especially if they also smoke cigarettes. Behavioral and medical interventions are highly warranted for such individuals.

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