

Moderate wine consumption and cancer risk in context

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Abstract. There is no doubt that excessive consumption of alcoholic beverages and binge drinking patterns increase the risk for cancer and many other diseases. Regarding the safety of light to moderate consumption of wine/alcoholic beverages, however, mixed messages exist. For decades, the potential health benefits of moderate wine consumption have been consistently shown, in particular for reducing cardiovascular mortality and morbidity. On the other hand, some population studies suggested that there is no safe limit of alcohol and ANY consumption is harmful to health, because of an increased cancer risk. Cancer is a multifactorial disease and it is increasingly accepted that certain lifestyle choices can affect the risk of developing cancer. Individuals do not drink only wine/alcoholic beverages, they eat different foods and have particular lifestyle habits. Besides several unmodifiable risk factors (age, sex, ethnicity and genetic disposition), improving lifestyle habits may contribute to reduce the risk of cancer. According to the World Health Organisation (WHO) and the World Cancer Research Fund (WCRF), one third of the cancers could be prevented by adopting a healthy lifestyle (such as avoiding smoking, maintaining a normal body weight, being physically active, avoiding excessive consumption of alcoholic beverages and keeping a healthy dietary pattern). Furthermore, the Mediterranean Diet is considered as one of the healthiest in the world by the WHO and is directly associated with a lower rate of mortality thanks to its effects on disease prevention. However, moderate consumption of wine is an important component of that diet. So recommendations for a healthy lifestyle which include a healthy, balanced diet and avoidance of any alcoholic beverage may be confusing. Can moderate wine drinkers still enjoy a glass of wine with the meal without jeopardizing their health? A detailed analysis of the scientific evidence will be provided and the risk of moderate wine consumption within the context of lifestyle will be examined.

While existing research is largely consistent regarding the harms of heavy/excessive drinking and binge drinking in terms of both cancer risk and overall mortality, there are disparate messages regarding the safety of light to moderate consumption of wine/alcoholic beverages [1,2].

Cancer is one of the leading causes of death. Due to the oxidative compounds caused by alcohol metabolism, cells are more prone to mutations and therefore a direct link to cancer is assumed [3]. Many organizations advocate zero alcohol consumption to prevent various cancers. They argue that there is ‘no safe limit of alcohol’, mainly based on an increased cancer risk [4-8], without assessing the pattern of consumption, the type of alcoholic beverage and other lifestyle factors. The authors concluded that it would be best for the overall health to avoid drinking at all, despite the fact that a reduced risk of myocardial infarction and of all-cause mortality was found, and that cardiovascular diseases are the number one cause of death [9].

On the other hand, for decades, the potential health benefits of moderate wine consumption have been consistently shown, in particular for reducing cardiovascular mortality and morbidity [10]. The J-curve has been established, where moderate drinkers are at a lower risk of chronic diseases (such as coronary heart disease) and death from all causes than either abstainers or heavy drinkers. Cohort studies have found that low or moderate consumption of alcoholic beverages is associated with a lower risk of cancer than the abstainer group [3, 11-13].

Yet in a recent publication, the same authors who argued that ANY consumption is harmful to health contradict their previous results and conclude that

moderate consumption of alcoholic beverages is associated with a lower risk of some disease outcomes and some health benefits in adults over the age of 40 years [14].

There seem to be quite a few inconsistencies, which add to the complexity and controversy in the scientific literature and provoke respective headlines in the media, which contribute to the confusion of health professionals and consumers.

What does it mean in practical terms for physicians advising their patients and for the average consumer? Can a glass of wine still be enjoyed with the meal without jeopardizing one’s health? The objective is to examine the current scientific evidence and assess a possible cancer risk when wine is consumed moderately in the context of a healthy lifestyle.

1 Is there a difference between alcoholic beverages?

The overall cancer risk is difficult to evaluate since it takes a long time for the cancer to develop and many factors contribute to the cancer development [15]. The extent to which alcoholic drinks can be a cause of various cancers depends on the amount of alcohol consumed and how it is consumed, some epidemiological studies have also identified the type of alcoholic beverage consumed [16].

A large meta-analysis examined the association between alcohol intake (without distinguishing between the types of alcoholic beverages) and cancer risk. For a moderate consumption of up to 1 drink/day, no increased risk of the most common cancers was found, except for the relatively small increase in the incidence of breast cancer in women and colorectal cancer in men [17]. Another large

prospective study found a J-shaped association between alcohol and mortality when examining the lifetime alcohol consumption in older adults, which remained after adjusting for the cancer risk. The lowest combined risk of death and cancer was observed for light alcohol intakes (between 1 and 5 drinks/week¹) in both men and women [18]. An assessment of risk for all cancer types by pooling the results of several epidemiological studies in a meta-analysis found a J-shaped curve between light to moderate drinking and overall cancer risk. This translated into a 9% lower risk of developing cancer for light drinkers (<12.5 g alcohol/d) compared to abstainers but an increased risk for excessive drinkers. No increased mortality risk of cancer for moderate drinkers (1-3 drinks/day) compared to abstainers [19] was reported. In an attempt to quantify the effect of moderate consumption of alcoholic beverages on overall cancer incidence in the Western world [20], another meta-analysis concluded that moderate drinking had no substantial impact on overall cancer risk.

In this context, it is important to remember that the risk of developing cancer involves various risk factors and all cancers that have been associated with alcohol also occur in the absence of drinking.

Some of the meta-analyses investigating the association between the consumption of alcoholic beverages and cancer risk have limitations that need to be considered when evaluating the cancer risk. The assessment of the different drinking patterns and types of alcoholic beverages in modifying the effect of the total amount of alcohol may be missing [21] and in addition, underreporting of alcohol consumption may partly or largely explain the cancer risk with light drinking [22].

2 The importance of context – lifestyle factors

It is increasingly accepted that certain lifestyle choices can affect the risk of developing cancer. Individuals do not drink only wine/alcoholic beverages; they eat different foods and have particular lifestyle habits. Besides several unmodifiable risk factors (age, sex, ethnicity and genetic disposition), improving lifestyle habits may contribute to reduce the risk of cancer. According to the World Health Organisation (WHO) and the World Cancer Research Fund (WCRF) [23], one third of the cancers could be prevented by adopting a healthy lifestyle (such as avoiding smoking, maintaining a normal body weight, being physically active, avoiding excessive consumption of alcoholic beverages and keeping a healthy dietary pattern) [24,25].

Furthermore, the Mediterranean Diet (Med Diet) is considered as one of the healthiest in the world by the WHO, that notes that it is directly associated with a lower rate of mortality thanks to its effects on disease prevention [26]. However, moderate consumption of alcoholic beverages, particularly wine, is an important component of that diet. So how do these recommendations for a 'healthy' lifestyle, which include a healthy diet and avoidance of alcohol, fit into the Mediterranean Diet perspective?

Since cancer is a multi-factorial disease, the cancer risk cannot be evaluated in isolation, and studies suggest that lifestyle factors are important risk factors for cancer [27]. Accordingly, the consumption of alcoholic beverages cannot be accurately evaluated in isolation from the other risk factors. The effect of alcohol on cancer risk will depend on the context, such as alcohol with or without a meal, the type of foods consumed as well as smoking at the same time [16].

When the risk from alcohol is assessed within the context of a balanced diet and a healthy lifestyle, the results seem to be very different. Indeed, the balance between genetic predisposition and environmental factors, including nutritional components and lifestyle behaviours, determines individual susceptibility to develop cancer [28].

Smoking (30%), obesity (20%) and infections (15%) appear to account for a large proportion, while physical inactivity, an unhealthy diet and occupational hazards contribute 5% each. The excessive consumption of alcoholic beverages contributes 3% to the overall cancer incidence [29]. Thus, it is important to evaluate the cancer risk in context with its cultural, drinking and eating patterns and lifestyle influences, and also remember that epidemiological studies cannot adequately control for all possible confounding factors such as social background, education, physical activity, eating and drinking pattern, and other unknown factors.

When these confounding factors are not adjusted in the research, the cancer risk can be completely different. Long-term observational studies have also found differences between the alcoholic beverages. At low to moderate wine consumption, often no association with alcohol-related cancer types was observed [30,31]. For example, distinguishing between the types of alcoholic beverages was reflected in the cancer risk: in contrast to beer and spirits consumers, where the cancer risk increased significantly in a dose-dependent manner, in wine drinkers, no increased cancer risk was observed [32].

Being physically active can mitigate the (all-cause and) cancer mortality risks associated with the consumption of alcoholic beverages. A British study showed a dose-response association between the intake of alcoholic beverages and cancer mortality in inactive participants but not in physically active participants [33].

3 Moderate wine intake in the Mediterranean diet and cancer risk

Many studies have focused on determining a safe level of alcohol intake, resulting in mixed results from abstinence to moderate consumption [34-37]. However, rather than looking at each individual component, more focus should be on the overall patterns of consumption [3]. Many prospective studies reported a greater benefit from adhering to a Mediterranean dietary and drinking pattern than from the intake of a particular nutrient [38-41]. The antioxidant components of the diet and wine may reduce the carcinogenic effect of ethanol [3,42].

¹ One glass of wine = approx. 147 ml = approx. 14 g of alcohol.

The Mediterranean drinking pattern is not only about the amount of alcoholic beverage consumed but also the type of alcoholic beverage predominantly consumed – wine - and how it is consumed. Drinking patterns in terms of frequency and the amount of wine consumed as well as drinking with or without a meal are important influencing factors for the biological effects. Spanish researchers examined the drinking patterns and concluded that the traditional Mediterranean drinking habits (moderate intake of wine/alcoholic beverages, spread over the week and consumed during meals, low spirit consumption, and avoidance of binge drinking) were also associated with a lower risk of all-cause mortality [43].

Risky and harmful drinking patterns including the regular excessive consumption of wine, as well as consuming heavy and excessive amounts on a single occasion (binge drinking), should be avoided. It is best to drink wine as an accompaniment to food, and alternate it with a non-alcoholic beverage such as water [44].

When light to moderate wine consumption was assessed in the context of a Med Diet and other lifestyle factors, no increased cancer risk was observed [10,30,31]. The extent to which different drinking and dietary patterns, lifestyle habits and/or beverage specific ingredients are responsible for the observed reduced risk of certain cancers continues to be discussed, and may provide an explanation as to why no increased breast cancer risk has generally been observed within the context of a Mediterranean Diet [31,45-50]. When examining moderate wine consumption in the context of the Mediterranean diet and typically with the meals, no increased cancer risk, even for breast cancer [30,47] was found. Furthermore, a better adherence to the Med Diet was also associated with a lower risk of total mortality [51].

The above results were confirmed by large meta-analyses, where a greater adherence to the Med Diet was associated with a lower cancer risk [30,31,52]. When focusing specifically on prospective trials, this meta-analysis highlighted a lower risk of suffering colorectal and breast malignancies and cancer mortality among subjects with a high adherence to the Med Diet. In line with these findings, a randomized controlled trial has studied the effect of this dietary pattern on cancer incidence. Adherence to the traditional Med Diet in the context of the PREDIMED Study demonstrated a decrease in the development of all sub-types of breast cancer and a decrease in its recurrence [47]. Such results need to be confirmed in further long-term trials.

As stated by Schwingshackl et al. [30], the attribution of anti-cancer effects to alcohol consumption seems controversial, considering that it is categorized by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogen for humans [53] and by the World Cancer Research Fund as a convincing carcinogen for mouth, pharynx, larynx, esophagus, stomach, liver, colorectal, and breast malignancies [54]. Low-to-moderate wine consumption contributes, however, to a higher Med Diet adherence (linked to the previously described benefits) and no dose-response effect of the toxicity of

alcohol or wine consumption can be inferred from their conclusions.

4 Wine - a special component

The inclusion of alcohol in the Med Diet usually refers to moderate wine consumption as part of a meal [43]. When analysing the components of the Med Diet that contributed most to such a decreased cancer risk, researchers have specifically identified the moderate, but not excessive consumption of alcoholic beverages and predominantly wine as well as fruits, vegetables and whole grains as protective components [30,55].

There is sufficient clinical evidence to point out that moderate wine drinkers have a lower risk for cancer compared to drinkers of other alcoholic beverages. So far, the anti-cancer effects of wine-specific polyphenols have only been observed in animal and laboratory studies. In some epidemiological studies, however, the risk of cancer has been shown to be lower in wine drinkers than in those who consumed other alcoholic beverages [32,56,57]. Wine provides large amounts of several bioactive compounds - polyphenols - that may be potentially responsible for some of the wine's anti-cancer effects [58]. The possible counter effects of the entire dietary composition of a Med Diet against the toxicity of alcohol on cancer has not been explored [59]. Thus, the observed positive health effects of light to moderate wine consumption may be - at least in part - linked to the protective effects of specific bioactive ingredients in wine (polyphenols) as well as in the foods consumed, with higher abundance in the Mediterranean diet [30,31,55].

5 Cancer risk in the context of lifestyle

Other lifestyle factors can also contribute to a lower cancer risk. Several studies confirm that adopting a healthy lifestyle and a balanced diet, including a moderate consumption of wine/alcoholic beverages, has a number of positive and protective health effects.

A large study from Harvard University [10] has shown that five lifestyle factors could increase life expectancy. One of these five lifestyle factors - a moderate intake of alcoholic beverages - was defined for women 5-15 g of alcohol/day or the equivalent of 50 to 150 ml of wine and for men, 5-30 g of alcohol/day or the equivalent of 50 to 300 ml of wine. The same Harvard researchers examined how multiple lifestyle factors relate to life expectancy without major diseases [60]: following a healthy lifestyle at mid-life is associated with a longer life span and a lower risk of major diseases such as cancer, cardiovascular and diabetes. The study highlights five specific lifestyle factors: besides a healthy diet, these include not smoking, being physically active, keeping a normal body weight and a moderate consumption of wine/alcoholic beverages.

A large European study reported similar results [61]: the higher the number of healthy lifestyle habits, the longer the lifespan without major chronic diseases (type 2 diabetes, coronary heart disease, stroke, cancer, asthma, chronic obstructive pulmonary disease, heart failure, dementia). The longest lifespan free of disease was

observed among those participants with a normal weight (BMI < 25) and two of the following lifestyle factors: never smoking, physical activity and moderate consumption of alcoholic beverages (1-14 drinks per week for women and 1-21 drinks per week for men²).

6 Conclusions

Failing to account for confounding factors, the estimated intake of a given amount of alcohol provides an incomplete assessment of its effects on health. The cultural context as well as drinking and eating patterns as well as other lifestyle factors are not accounted for in modelling studies, where data from many diverse countries are pooled together. Those meta-analyses rely on many assumptions (ie. actual consumption data of alcoholic beverages are not available and the consumption is calculated from sales data instead) and the statistical modelling applied cannot capture the confounding factors, when they haven't been accounted for in the studies that provide the basis for the statistical models. Because of these limitations, those type of studies cannot provide an estimate of the individual cancer risk. When the context of alcohol consumption has not been taken into account appropriately, then there is the risk that responsible drinking will be stigmatised.

However, considering the scientific evidence of wine/alcohol consumption in the context of the Mediterranean diet and a healthy lifestyle, no increased risk with light to moderate intake is observed. There are not enough data to support an increased risk of cancer when wine is moderately consumed during the meals and as part of a Mediterranean diet and healthy lifestyle. Such a drinking and dietary pattern seems to result in more health and societal benefits than harm.

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² One drink being equivalent to 10 g of alcohol.

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