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EDITORIAL

# Alcohol and cancer: no threshold exists

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It has been estimated that in 2018 worldwide new cancer cases reached 18.1 million and that 9.6 million were deaths.[1]

Alcohol consumption is one of the major risk factors:[2] around 5% of all cancers are attributable to alcohol.[2] Shield *et al.* reported at least 80,000 alcohol-related cancer deaths in Europe, in 2016.[3] In France, alcohol is in second place as risk factor for oncological death, immediately after tobacco smoking.[4] It is conceivable that these data are underestimated: it is known, in fact, that adequate anamnestic attention about drinking habits is lacking in clinical practice.

Ethanol present in all types of alcoholic beverages (wine, beer, spirits) has a certain causal correlation with the following types of cancer: oral cavity, oropharynx, hypopharynx, colon, rectum, liver, larynx and breast female. The International Agency for Research on Cancer (World Health Organization),[5] World Cancer Research Fund International (WCRF)[6] and the Institute National du Cancer France (INCF)[7] agree on this consideration. The causal relationship with esophageal cancer is supported by the International Agency for Research on Cancer. As for stomach cancers, gallbladder, pancreas and prostate to date, the data are still controversial.[1]

Acetaldehyde, a product of ethanol metabolism, has a certain causal relationship with head and neck cancers. Free acetaldehyde is present in all alcoholic beverages in varying quantities.[5] The relationship is dose dependent. The greater cancer risks are concentrated in the moderate-heavy drinker categories. However, for some types of cancer the risk is already present with light dosages (about 10 g/day of ethanol). Some example is that of the oral cavity and pharynx (1.13; 95% confidence interval [CI] 1 to 1.26), esophageal squamous cell carcinoma (1.26; 95% CI: 1.06 to 1.50), female breast (1.04; 95% CI: 1.01 to 1.07).[1] The female breast is certainly the organ most sensitive to ethanol-induced damage. The American Society of Clinical Oncology (ASCO) estimated a 5% increase in premenopausal breast cancer per 10 grams of ethanol consumed per day (pooled risk ratio [RR], 1.05; 95% CI: 1.02 to 1.08). The risk was greater for postmenopausal breast cancer (RR 1.09; 95% CI: 1.07 to 1.12) for each 10 grams of ethanol per day.[8] The risk increases in presence of genetic polymorphisms (up to 27%). There are several polymorphisms, involved in estrogen synthesis and metabolism, such as in CYP17, CYP19, CYP1B1, and the Catechol-O-methyltransferase, which have been associated with increased breast cancer risk.[9] Not only alcohol increases the risk of developing breast cancer but it may also increase the risk of breast cancer recurrence and death following breast cancer onset.[9] Drinking 6 or more grams of alcohol per day compared with no drinking

is possibly associated with an increased risk of breast cancer recurrence and death from breast cancer. Regular drinking equivalent to two to four standard drinks or more per week is associated with 1.3-fold and 1.5-fold increased risk of breast cancer recurrence and breast cancer death respectively. The association appears stronger among postmenopausal women and overweight/obese women separately. Despite the fact that alcohol intake is one of the few modifiable breast cancer risk factors yet identified, Chambers *et al.* reported that "Many (women) considered alcohol advice irrelevant as the association with breast cancer was largely unknown, and they did not consider their drinking to be problematic."[10]

Alcohol consumption worsens outcomes among patients undergoing surgery for oncological causes: longer hospitalizations, an increase in the number of surgical procedures, an increase in costs and an increase in mortality.[8]

The alcohol-cancer ratio is clear; however, the alleged beneficial effect of light-moderate dosages is a confounding factor. In reality, it is known that alcohol consumption is linearly related to increased blood pressure, arrhythmia (mainly atrial fibrillation), and hemorrhagic stroke.[9] Important meta-analyses failed to demonstrate a beneficial effect on all causes of mortality for low-volume alcohol use compared with abstinence. This suggests the lack of a real benefit to daily alcohol consumption.[8] This is highlighted by Stockwell *et al.*, who reported that "Estimates of mortality risk from alcohol are significantly altered by study design and characteristics. Meta-analyses adjusting for these factors find that low-volume alcohol consumption has no net mortality benefit compared with lifetime abstention or occasional drinking".[11]

It is clear that even if there is a real beneficial effect for some pathologies, with the same dosage the risk of cancer increases. Hence, it is anachronistic attitude to continue affirming that the alcohol and cancer ratio is a question of dosage. It is good to underline, however, that professional experience teaches us that people who consume alcohol defend their drinking. Therefore, even the health professional who consumes alcohol is less likely to discourage its use. In a Danish study, 18.8% of physicians meet the criteria for risky consumption.[12] Other estimates indicate that around 14% of American physicians will have alcohol use disorders during their lifetime.[13]

The position of the Italian Society on Alcohol is to discourage alcohol consumption in general and in particular in subjects who have a positive oncological familiarity or who have already had a first diagnosis of cancer. Abstention is the scientifically best solution, however in patients with high consumption an initial reduction in dosage can be an acceptable bridge to abstinence and also reduces the risk of clinical complications including cancer. Roereche et al found that reducing from 14 to 11 alcoholic beverages per day decreases the risk of mortality by about 10 times, as does reducing 3 to 0 alcoholic beverages per day.[14]

In conclusion, the Italian Society on Alcohol is in agreement with what it claims the American Society of Cancer Oncology "the risk of cancer is increased even with low levels of alcohol consumption, so the net effect of alcohol is harmful. Thus, alcohol consumption should not be recommended to prevent cardiovascular disease or all-cause mortality"[8] and with what was said by the European Code Against Cancer which represents the correct synthesis that to date the scientific evidence makes available to us: "if you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention."[15]

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