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Editorial

NUTRITION AND RISK OF CANCER: A CHALLENGE FOR RESEARCH AND CLINICAL PRACTICE

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Cancer represents an important public health issue posing a significant burden on patients, caregivers and society. According to the International Agency for Research on Cancer (IARC), in 2012 were recorded worldwide 14.1 million new cancer cases and 8.2 million deaths were attributable to cancer [1], thus positioning cancer among the 10 leading causes of death [2]. By gender, in 2012, 52% of the new cancer cases were reported in men, accounting for an age-standardized incidence rate of 205 cases/100,000 person-years [1]. In women, this age-adjusted rate was lower - 165 cases/100,000 person-years [1]. While in both genders the incidence rate has been reported to vary according to geographical region and income per country, with lower rates in less developed regions and higher rates in the most developed ones, less variation was observed in mortality rates [1].

Studies on regional variations of cancer incidence, lifestyle factors, occupational and environmental exposures to carcinogens have shown that up to 60% of the cancer deaths are preventable [3,4]. Among the incriminated carcinogens that could be avoided tobacco exposure is probably the most known example and its link to laryngeal, lung, oral, bladder, cervical, oesophageal, kidney, and pancreatic cancers is well known [5,6]. Asbestos, arsenic, and chronic infections with hepatitis B, C and human papilloma virus, are just a few examples of other preventable causes of cancer [7].

Following the research on the link between lifestyle and cancer and the increasing number of evidence for an association between diet components and oncogenesis, oncology nutrition has emerged as a specialized field of nutrition playing a key role in prevention and treatment of cancer [8,9]. According to the World Cancer Research Fund International (WCRFI), "about a third of the most common cancers are preventable through a nutritious diet, maintaining a healthy weight and regular physical activity" [10]. Here we are providing a brief summary of the existing evidences on the link between various cancer types and diet with a focus on the most frequent forms of neoplastic disease.

Nutrition status

Adult weight gain, body fatness, overweight, obesity and the abdominal distribution of

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adipose tissue have been associated with an increased risk for several types of cancer, decreased survival and increased recurrence of the disease, and decreased quality of life in cancer survivors [9,11]. The pathogenetic mechanisms hypothesized to be involved in the relationship between body fatness and cancer risk are the inflammatory response, oxidative stress, and increased level of circulating oestrogens induced by insulin resistance, hyperinsulinemia, increased IGF-1 levels and increased production of adipokines by the adipose tissue [9,12]. Of all cancer types, overweight and obesity have been shown to increase the risk of adenocarcinoma of the oesophagus, gastric, pancreatic, endometrial, ovary, prostate, kidney, gallbladder, liver, bowel and breast cancer in post menopause [9]. Abdominal distribution of adipose tissue has been associated with an increased risk of colorectal cancer, and weight gain at adult age has been associated with an increased risk of oesophageal, thyroid, colon and kidney cancer in men and with an increased risk of endometrial, gallbladder, kidney and oesophageal cancer in women [9,13]. A meta-analysis including 9 studies and 1725 oesophageal cancer cases published by the WCRFI showed that for every 5 kg/m² increase in BMI the risk of oesophageal adenocarcinoma increased with 48% (RR = 1.48 [95% CI 1.35–1.62]) [14]. For every 5 kg/m² increase BMI the risk of cardia cancer increased with 23% (RR = 1.23 [95% CI 1.07–1.40]) [15], of kidney cancer and liver cancer with 30% (RR 1.30 [95% CI 1.25–1.35] [16], respectively RR 1.30 [95% CI 1.16-1.46] [17]), of gallbladder with 25% (RR 1.25 [95% CI 1.15–1.37]) [18], of prostate cancer with 8% (RR 1.08 [95% CI 1.04-1.12]) [19], of endometrial cancer with 50% (RR 1.50 [95% CI: 1.42-1.59]) [20], and of pancreatic cancer with 10% (RRs 1.10 [95% CI 1.07-1.14]) [21].

Nutritional factors associated with an increased risk of cancer

The consumption of energy-dense food and sugary drinks promotes weight gain, overweight and obesity and through this increases the risk of several cancers [9], as described above.

Red and processed meat consumption, such as the meat preserved by smoking, curing, or salting, or by the addition of preservatives (e.g. nitrates, nitrites, salt), has been shown to be associated with an increased risk of non-cardia stomach cancer (only processed meat), and colorectal cancer [15,22]. A meta-analysis of 3 studies performed by WCRF showed that the consumption of 50 grams of processed meat/day is associated with 18% higher risk of non-cardia cancer (RR = 1.18 [95% CI 1.01–1.38]) [15]. The consumption of processed meat was associated with 18% and 24% higher risk for colorectal and colon cancers for every 50 g of processed meat consumed/day; while the consumption of red meat per se was associated with 17% higher risk of colorectal cancer [21]. The carcinogens incriminated in the link between processed meat and cancer are the N-nitroso compounds derived from the nitrites and nitrates added in processed meat; salt (for gastric cancer; mechanism discussed below); heterocyclic amines and polycyclic aromatic hydrocarbons results from high temperature cooking; production of free radicals favoured by iron contained in the red meat [9,15,22,23].

High salt intake has been shown to favour *Helicobacter pylori* colonization, a risk factor for gastric cancer [24]. However, meta-analyses established a direct link only between salt-preserved food and risk of gastric cancer (e.g. 9% higher risk for each 20 g of salt-preserved vegetable consumed/day) and not with the amounts of salt/day, raising the question if this consumption is not a bystander of the socio-economic status with limited access to other methods of preservation [15].

Alcoholic drinks consumption has been incriminated as a risk factor for several cancers. For stomach cancer, the risk was significantly higher starting from 45 mg ethanol consumed /day (8% increase in risk) and reached 28% increase in risk in those reporting a consumption of 120 mg ethanol/day [15]. For the colon cancer, the consumption of 10 g ethanol/day was associated with 11% higher risk of colorectal cancer in men; however, the evidences are inconsistent in women [22]. Increased ethanol consumption has been also associated with a higher risk of breast cancer (10% increase for 10 mg ethanol/day) [9], liver (4% increase for 10 mg ethanol/day) [17], oesophagus (25% increase for 10 mg ethanol/day) [14], mouth, pharynx and larynx cancers (3% increase for 1 drink/week) [9]. Among mechanisms incriminated are the production of free radicals, increased carcinogens penetration in the mucosa due to solvent properties of ethanol, and direct action of acetaldehyde, a known carcinogen [15,25].

Other factors for which there are consistent evidences of increased cancer risk are:

Glycaemic load has been shown to increase the risk of endometrial cancer with 15% for 50 units/day [20].

Aflatoxins, which may contaminate grains and vegetables, have been shown to be associated with 54% to 500% higher risk of liver cancer [26,27].

High doses beta-carotene supplements in smokers are associated with higher risk of lung cancer [9].

Nutritional factors associated with a decreased risk of cancer

Several foods or food components have been shown to have a protective effect against the occurrence of some forms of cancer.

Higher fruit and vegetable intake was found to be associated with lower risk of colorectal cancer, but the protective effect varies among studies, from a non-significant 9% risk reduction to a reduction of 14% in risk of colorectal cancer and a reduction of 24% in risk of colon cancer [28]. Dietary fibers from fruit, vegetable and whole grain cereals were also been shown to be associated with lower risk of colorectal cancer but not all studies confirmed this beneficial effect. Some studies reported that intakes between 33.1 and 12.6 g/day can decrease the risk with up to 25% [28]. A meta-analysis including 25 prospective studies demonstrated that each 10 g of fibers/day decreased the risk with 10 % (RR 0.90 [95% CI 0.86-0.84]), but the inverse association was statistically significant only for colon cancer and not for rectal cancer [29].

In a meta-analysis including 15 prospective studies and 900.000 participants it was found that in men consuming 525 g/day of nonfermented milk, the relative risk for colon cancer decreased by 26%, but the protective effect was neither found for rectal cancer in men nor for colon or rectal cancer in women [30]. Other food components mentioned as having a ‘probable’ protective effect in bowel cancer is calcium and garlic [22].

Alcoholic drinks in an amount of up to 30 g/day (2 drinks) are considered to have a ‘probable’ protective effect on the occurrence of kidney cancer, but not in higher amounts [16,31,32]. The possible mechanisms involved in this protective effect are the decrease in insulin resistance and risk of type 2 diabetes, the presence of antioxidant phenolic compounds in alcoholic beverages, and the diuretic effect of alcohol which may reduce exposure to carcinogens [16]. It is worth mentioning that alcohol use is associated with increased risk for numerous other types of cancer as discussed above.

Based on the results of three recent meta-analysis, an inverse relationship between coffee

consumption and risk of liver cancer has been confirmed [17]. The dose-related protective effect was found to be variable: one cup per day was associated with a risk decrease of 17% [33], the heaviest coffee consumers had a 52% less risk than those who never or almost never consumed coffee [34] and two cups per day were associated with a 44% risk reduction [35]. Coffee contains numerous components which are thought to exert effects on stimulating the endogenous defence system, DNA repair, and reduce the expression of genes involved in inflammation among other possible mechanisms [17].

To conclude, nutrition and cancer remains a subject of interest for researchers but also for practitioners involved in the care and prevention of cancer. Not at last, patients suffering from cancer and general public have always manifested a deep interest in the relationship between nutrition and cancer and scientifically-based answers are clearly needed.

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