

Nutritional habits and bladder cancer

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It is now universally acknowledged that nutrition has a paramount importance in health and disease (1). Cancer is probably one of the most paradigmatic example of a human pathology whose risk of development and progression may be strongly influenced by different dietary habits, through intricate and multifaceted mechanisms entailing a kaleidoscope of still partially enigmatic interplays among genetic, epigenetic, biochemical and also gut-microbial factors (2).

According to recent statistics, bladder cancer is the fifth more frequent malignancy (i.e., approximately 4.7% of all cancers) and the seventh cause of mortality for cancer (2.8% of all cancer deaths), in both sexes (3). The frequency of this cancer is greater in men (i.e., representing the third more frequent malignancy in the male gender), is the highest in North America and Europe, and its pathogenesis has been convincingly associated with many environmental factors such as cigarette smoking, infections (i.e., schistosomiasis), workplace exposures to aromatic amines (e.g., benzidine and beta-naphthylamine), intake of certain drugs (e.g., pioglitazone) or dietary supplements containing aristolochic acid, prior chemotherapy or radiation therapy, and arsenic exposure (4). Some genetic factors have also been associated with an increased risk of developing bladder cancer, mainly represented by polymorphisms in genes encoding for glutathione S-transferase M1 (*GSTM1*) and N-acetyltransferase 2 (*NAT2*) (4).

The relationship between dietary habits and bladder cancer is by far more enigmatic. A critical review of the

literature, very recently published by Fankhauser and Mostafid, showed that there may be an association between this malignancy and certain foods such as fruits, vegetables, meat, milk products and oil, but also concluded that no reliable evidence exists that a specific diet may be really effective in lowering bladder cancer risk (5). Piyathilake recently gave a nice overview on dietary factors potentially associated with bladder cancer, and confirmed that no strong evidence exists that specific dietary habits, or supplementation with micronutrients, may be effective in reducing bladder cancer risk (6).

In a recent article, Westhoff *et al.* provided some valuable insights on the still unclear relationship between nutrition and bladder cancer (7). The authors published the results of a large cohort study based on 595 patients with newly diagnosed non-muscle-invasive bladder cancer, who were followed-up for a median period of 66 months. Notably, patients in the highest tertile of adherence to a Western dietary pattern had a 48% higher risk of recurrence of bladder cancer (hazard ratio, 1.48; 95% confidence interval, 1.06–2.06) when compared to patients in the lowest tertile, whilst no other statistically significant associations were found between other dietary habits and the risk of progression or recurrence. The so-called Western diet is especially low in fresh fruits and vegetables, but generally high in saturated fats (i.e., fried foods) and red and processed meat, which are associated with a plethora of malignancies. In particular, convincing associations have been reported between high intake of red

Table 1 Epidemiologic associations between certain foods and risk of bladder cancer

Positive associations (higher consumption = enhanced risk)	
❖	Meat (especially red and processed)
❖	Fats and saturated fats (especially fried foods)
❖	Eggs
❖	Coffee
Negative associations (higher consumption = decreased risk)	
❖	Cruciferous vegetable
❖	Citrus fruits
❖	Green tea

and processed meat with colorectal, lung, esophageal and gastric cancer (8), and also between high consumption of saturated fats (especially fried foods) and prostate, breast, endometrium and ovary cancers (9,10). Notably, a Western diet has also been straightforwardly associated with other, highly prevalent and severe human pathologies, such as cardiovascular disease (11) and diabetes (12), among others.

Albeit the results of the prospective study of Westhoff *et al.* (7) need to be confirmed in larger prospective investigations, such as the ongoing BLEND (bladder cancer, epidemiology and nutritional determinants) study (13), some clear-cut implications can be drawn. On the assumption that a healthy diet may have a putative impact in reducing the risk of development and progression of bladder cancer, as well as on lowering the risk of developing many other human disorders, a list of foods, whose consumption may be increased or reduced, can be envisaged (*Table 1*) (6,14-16). Intriguing associations with a reduced bladder cancer risk have also been observed with certain vitamins, especially vitamin B, C, D and E, so that supplementation with these micronutrients may be considered for lowering the overall risk of developing this frequent type of cancer (6,14-17). These general considerations are strengthened by recent evidence that adherence to standard dietary recommendations is quite scarce in bladder cancer survivors (18).

One of the future steps researchers will have to consider in the race to unravel the link between diet and bladder cancer will undoubtedly be built over the urinary tract microbiota. If for years urine has been considered an almost sterile biological fluid, it is now very well known that microorganisms present at urinary tract level have a role in maintaining urinary health (18). Actually, dietary

choices may drastically influence the urinary tract microbial ecosystem (19), as, for example, specific urinary metabolites of compounds introduced through a diet rich in plant foods may be bacteriostatic or even show antibiotic activity (20). For this reason, a deeper investigation of the urinary microbiota, and on how it can be influenced by dietary choices, will reasonably lead us to rethink the preventative approaches for bladder cancer.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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