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Dietary water intake and bladder cancer risk: An Italian case–control study

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ABSTRACT

Previous studies on the relationship between fluid intake and risk of bladder cancer have generally focused on beverages, and results have been inconsistent. We investigated the relationship between water intake and bladder cancer risk, considering water from both beverages and foods.

Between 2003 and 2014 we conducted a multicenter hospital-based case–control study in Italy on 690 cases and 665 frequency-matched controls. Water intake for beverages and foods was computed using the Italian food composition database. Odds ratios (ORs) and the corresponding 95% confidence intervals (95%CIs) for water intake were estimated by unconditional multiple logistic regression models, adjusting for major risk factors for bladder cancer.

In the control group, the 64.7% of water intake derived from beverages and 35.4% from foods. Comparing the highest with the lowest quartile of intake, water from beverages (OR = 1.14; 95%CI: 0.82–1.59) and water from foods (OR = 0.88; 95%CI: 0.61–1.28) were not significantly associated with bladder cancer risk. Some specific water sources showed significant associations with bladder cancer risk (e.g. water from vegetables, OR = 0.58; 95%CI: 0.40–0.86). However, these associations may be due to the effect of other components contained in beverages and foods rather than to the water content itself.

Considering the intakes of water from both beverages and foods, total water intake was not associated with bladder cancer risk.

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1. Introduction

In Europe, bladder cancer is the fourth most frequent cancer diagnosed in men, accounting for approximately 118,000 new cases each year [1]. This cancer is less common in women, with approximately 32,000 new cases each year. Transitional-cell carcinomas (TCCs) represent the most frequent histological type, accounting for over 90% of bladder cancers [2].

Tobacco smoking and occupational exposure to aromatic amines are the major recognized risk factors for this neoplasm [2–4]. Among dietary factors, fluid intake has been inconsistently related to bladder cancer risk [5]. Currently, the evidence on total fluid intake presents great heterogeneity across studies [5] and according to the type of beverage [6]. Different biological mechanisms have been put forward to clarify these potential relationships. As proposed by the "urogenous contact hypothesis" [7], an increase in fluid intake could reduce the risk of bladder cancer, since by impacting on voiding it could reduce the concentration of carcinogens in the urine and their contact time

Abbreviations: OR, odds ratio; CI, confidence interval; TCC, transitional cell carcinoma; G, grade.

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with the bladder epithelium. On the other hand, an increase in fluid intake may promote bladder distension and consequently introduce the carcinogens to the deep layer of the bladder and lead to a more intense contact between carcinogens and the bladder tissue [8]. Furthermore, beverages could contain components, carcinogens included, that may be responsible for the observed effect on bladder cancer risk [9,10], so that it may not be easy to disentangle their effect from that of water.

Investigations on fluid intake generally focused on beverages [11–16], thus not considering the fraction of water from fruit, vegetables and other foods. This is of particular relevance in testing the "urogenous contact hypothesis", since previous studies did not consider a relevant dietary source of water, which, in the Italian population, accounts for 20–40% of the total water intake, depending on the foods consumed [17].

The aim of the present study was to assess the impact of total water intake on bladder cancer risk, providing an estimate of water intake from beverages and foods, using data from an Italian case–control study.

2. Materials and methods

2.1. Subjects

Between 2003 and 2014, we conducted a case–control study on urothelial carcinoma of the bladder within an established Italian network of collaborating centers, including Pordenone and Milan in northern Italy, and Naples and Catania in southern Italy [18]. Cases comprised 690 patients aged 25 years or older (median age: 67 years; range 25–84 years) with incident bladder cancer diagnosis, admitted to major general hospitals in the catchment areas. Nearly all bladder cancer cases were confirmed by histological testing on tumor tissue specimens from biopsy or surgery, and three cases were confirmed by cytology only. Cases were stratified into two prognostic risk groups: (1) low-risk bladder cancers, including Ta WHO grade (G) 1 (well-differentiated) and Ta G2 (moderately differentiated) carcinomas; (2) high-risk bladder cancers, including in-situ carcinomas (CIS), T1–T4, and G3–G4 (poorly differentiated–undifferentiated) carcinomas [14]. Overall, 210 cases (30.4%) were classified into the low-risk prognostic group, 393 cases (57.0%) into the high-risk group, and 87 cases (12.6%) could not be determined because of an incomplete pathological record (Table 1).

Controls comprised 690 cancer-free patients admitted to the same network of hospitals as cases for a wide spectrum of acute conditions, unrelated to tobacco or alcohol consumption or long-term diet modification. Controls were frequency-matched to cases according to study center, sex, and 5-year age group. Twenty-five controls were excluded after enrolment because of inappropriate admission diagnosis, thus leaving 665 eligible controls (median age: 66 years; range: 27–84 years). Overall, 28.9% of controls were admitted for traumas, 22.1% for non-traumatic orthopedic disorders, 39.9% for acute surgical conditions, and 9.8% for miscellaneous other illnesses. All study subjects signed an informed consent, according to the recommendations of the Board of Ethics of the study hospitals.

2.2. Dietary assessment

Trained personnel administered a standard, structured questionnaire to study subjects during their hospital stay, with less than 5% refusal by both cases and controls. The questionnaire collected information on socio-demographic characteristics, anthropometric measures, lifetime smoking habit, and occupational exposure to selected chemical substances. Patients' dietary habits in the 2 years preceding study enrolment were collected through a validated and reproducible food-frequency questionnaire [19–22], including the following sections: (1) milk and sweeteners; (2) bread, cereals and first courses (including soups); (3) second courses (e.g., meat, fish, and other main dishes); (4) side dishes (vegetables and potatoes); (5) fruit; and (6) sweet and desserts. Four specific sections investigated lifetime consumption of beverages, assessing variations of at least one unit/day: (1) tap and bottled water; (2) alcoholic beverages (i.e., wine, beer, aperitif, hard liquor); (3) hot beverages (i.e., coffee, cappuccino, tea, herbal tea, and decaffeinated coffee); and (4) soft drinks (i.e., cola, energy, and other carbonated drinks). Consumption was reported in standard units: one glass of water (125 mL); one glass of wine (125 mL); one can of beer (330 mL); one glass of hard liquor (30 mL); one cup of coffee and decaffeinated coffee (30 mL); one cup of cappuccino, tea and herbal tea (125 mL); one can of cola and other carbonated drinks (330 mL); and one can of energy drinks (250 mL). Total energy and nutrient intakes, including water, were computed using the Italian food composition database [23]. To harmonize the difference

Table 1
Distribution of 690 bladder cancer cases and 665 controls, according to socio-demographic characteristics, body mass index, energy intake, smoking habit, and prognostic risk group. Italy, 2003–2014.

Variables	Cases		Controls		χ^2 test
	n	(%)	n	(%)	
Sex					
Men	595	(86.2)	561	(84.4)	
Women	95	(13.8)	104	(15.6)	
Age (years)					
<55	83	(12.0)	105	(15.8)	
55–59	65	(9.4)	73	(11.0)	
60–64	107	(15.5)	119	(17.9)	
65–69	164	(23.8)	147	(22.1)	
70–74	155	(22.5)	124	(18.7)	
≥75	116	(16.8)	97	(14.6)	
Study centre					
Pordenone	242	(35.1)	250	(37.6)	
Milan	241	(34.9)	238	(35.8)	
Naples	129	(18.7)	100	(15.0)	
Catania	78	(11.3)	77	(11.6)	
Education (years)[a]					
<7	292	(42.3)	273	(41.1)	
7–11	224	(32.5)	215	(32.3)	
≥12	173	(25.1)	177	(26.6)	$P = 0.80$
Body mass index (kg/m^2)[a]					
<25	249	(36.1)	223	(33.5)	
25 to <30	316	(45.8)	312	(46.9)	
≥30	125	(18.1)	129	(19.4)	$P = 0.60$
Smoking habit[a]					
Never	96	(13.9)	237	(35.6)	
Former	310	(44.9)	284	(42.7)	
Current					
<20 cigarettes/day	143	(20.7)	87	(13.1)	
≥20 cigarettes/day	132	(19.1)	57	(8.6)	$P < 0.01$
Energy intake (kcal/day)					
<1873	178	(25.8)	167	(25.1)	
1873 to <2233.9	164	(23.8)	166	(25.0)	
2233.9 to <2689	181	(26.2)	166	(25.0)	
≥2689	167	(24.2)	166	(25.0)	$P = 0.91$
Prognostic risk group[b]					
Low	210	(30.4)			
High	393	(57.0)			
Not determinable	87	(12.6)			

[a] The sum does not add up to the total because of missing values.
[b] Low-risk group includes Ta Grade (G) G1 and Ta G2 carcinomas; high-risk group includes in-situ carcinomas, T1–T4, and G3–G4 carcinomas.

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