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Re: Coffee Consumption and Prostate Cancer Risk and Progression in the Health Professional Follow-up Study

In a previous issue of the Journal, Wilson et al. (1) reported on data from the Health Professional Follow-up Study, which showed a negative association between coffee consumption and risk of prostate cancer, particularly lethal prostate cancer as defined by the authors. The report dealt with possible bias (eg, reverse causation) very carefully, and it reached conclusions at variance with previous null or positive associations (2). Confounding by tobacco smoking and lack of distinction between subsets of prostate cancer were mentioned as possible causes for the null associations found in previous studies (1).

To shed further light on this topic, we used data from a large Italian hospital–based case–control study (3) that assessed the relationship between coffee intake and risk of benign prostatic hyperplasia (BPH) and prostate cancer. The daily intake of regular and decaffeinated coffee during the 2 years preceding enrollment, together with information on smoking and drinking habits and other relevant variables (4), was assessed through a validated food-frequency questionnaire (5). Gleason scores could be retrieved from pathological records for 71% of patients with prostate cancer. Odds ratios were calculated by means of logistic regression models, adjusting for potential confounders.

We found no statistically significant associations between coffee consumption and the risk of BPH or prostate cancer (Table 1), and no differences were found when we stratified by tumor grade (ie, Gleason score 2–6, 7–10, or unknown). Tobacco smoking was not a likely confounder of our results, because no heterogeneous association between coffee intake and risk of BPH or prostate cancer emerged in strata of never, light, or heavy smokers.

The hypothesis that coffee may lower prostate cancer risk by reducing glucose response and improving insulin sensitivity (1) is an interesting one, because prostate cancer was positively associated with insulin level (6). However, this result needs further investigation because the stronger effect of coffee consumption on high-grade prostate cancer found by Wilson et al. (1) did not fully match the stronger association of insulin-like growth factor 1 with low-grade prostate cancer—rather than with high-grade prostate cancer—in the Health Professional Follow-up Study (7).

Studies from North America have tended to report negative associations between prostate cancer and coffee intake more often than studies from Europe (2). Differences in coffee consumption, coffee bean roasting, and brewing methods, as well as differences between prostate cancer–risk profiles among men in the United States vs those in Italy, could partly explain these differences (2). Our results suggested that smoking habits did not confound the association between coffee consumption and risk of prostate cancer. Nonetheless, other factors (eg, overweight), or variations in coffee consumption across different ethnic subsets of the US population, may have affected the findings from the Health Professional Follow-up Study (1).

Selection and recall biases cannot be ruled out in our study; however, fewer than 5% of eligible subjects refused to participate in our study and the questionnaire that we used had been successfully tested for reproducibility and validity (5). In addition, we were unable to restrict our analysis to lethal prostate cancer cases, as presented in the analysis of Wilson et al. (1). Nonetheless, our results do not lend support to a protective effect of high coffee consumption on prostate cancer or high-grade prostate cancer.

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Table 1. Odds ratio (OR) and 95% confidence intervals (CI) for benign prostatic hyperplasia and prostate cancer by daily intake of coffee*

	Coffee intake, cups/day										
	<1 (reference)		1–2			3–4			≥5			
Diagnosis	Cancer patients No. (%)	Control subjects No. (%)	Cancer patients No. (%)	Control subjects No. (%)	OR (95% CI)†	Cancer patients No. (%)	Control subjects No. (%)	OR (95% CI)†	Cancer patients No. (%)	Control subjects No. (%)	OR (95% CI)†	P_{trend} §
Benign prostatic hyperplasia												
All	201 (100)	217 (100)	686 (100)	730 (100)	0.98 (0.78 to 1.24)	398 (100)	413 (100)	1.12 (0.87 to 1.44)	84 (100)	91 (100)	1.31 (0.89 to 1.92)	.10
Smoking habits‡												
Never	78 (39.2)	61 (28.2)	242 (35.6)	201 (27.6)	0.83 (0.54 to 1.26)	96 (24.4)	74 (18.0)	1.05 (0.64 to 1.72)	8 (9.5)	8 (8.8)	1.16 (0.38 to 3.53)	.65
Ever, <20 cigarettes/day	60 (30.2)	84 (38.9)	262 (38.5)	276 (38.0)	1.25 (0.85 to 1.85)	155 (39.3)	157 (38.2)	1.31 (0.85 to 2.00)	26 (31.0)	23 (25.3)	1.72 (0.86 to 3.44)	.14
Ever, ≥20 cigarettes/day	61 (30.7)	71 (32.9)	176 (25.9)	250 (34.4)	0.85 (0.56 to 1.29)	143 (36.3)	180 (43.8)	0.99 (0.64 to 1.54)	50 (59.5)	60 (65.9)	1.11 (0.63 to 1.97)	.49
Prostate cancer												
All	185 (100)	217 (100)	671 (100)	730 (100)	1.05 (0.83 to 1.32)	371 (100)	413 (100)	1.11 (0.86 to 1.43)	67 (100)	91 (100)	1.05 (0.70 to 1.58)	.52
Gleason score												
2–6	70 (37.8)	217 (100)	284 (42.3)	730 (100)	1.16 (0.84 to 1.60)	155 (41.8)	413 (100)	1.23 (0.86 to 1.75)	29 (43.3)	91 (100)	1.15 (0.67 to 1.99)	.37
7–10	41 (22.2)	217 (100)	209 (31.1)	730 (100)	1.43 (0.97 to 2.10)	118 (31.8)	413 (100)	1.47 (0.97 to 2.22)	16 (23.9)	91 (100)	1.13 (0.58 to 2.23)	.33
Unknown	74 (40.0)	217 (100)	178 (26.5)	730 (100)	0.69 (0.50 to 0.96)	98 (26.4)	413 (100)	0.70 (0.48 to 1.02)	22 (32.8)	91 (100)	0.94 (0.52 to 1.70)	.34
Smoking habits‡												
Never	71 (38.6)	61 (28.2)	203 (30.4)	201 (27.6)	0.80 (0.53 to 1.23)	86 (23.3)	74 (18.0)	0.99 (0.60 to 1.64)	10 (15.2)	8 (8.8)	1.39 (0.47 to 4.11)	.71
Ever, <20 cigarettes/day	69 (37.5)	84 (38.9)	284 (42.6)	276 (38.0)	1.13 (0.77 to 1.66)	139 (37.7)	157 (38.2)	1.08 (0.71 to 1.65)	14 (21.2)	23 (25.3)	0.98 (0.45 to 2.16)	.94
Ever, ≥20 cigarettes/day	44 (23.9)	71 (32.9)	180 (27.0)	250 (34.4)	1.22 (0.78 to 1.92)	144 (39.0)	180 (43.8)	1.36 (0.85 to 2.19)	42 (63.6)	60 (65.9)	1.26 (0.68 to 2.32)	.33

* The study included 1369 patients with benign prostatic hyperplasia, 1294 with prostate cancer, and 1451 control subjects from the same hospitals. Coffee intake in the 2 years preceding study enrollment was assessed through a validated food-frequency questionnaire, administered by trained nurses to study subjects during their hospital stays.

† Odds ratios were calculated by means of logistic regression models, adjusting for center (Aviano, Gorizia, Milan, Naples, and Latina), age (<50, 50–54, 55–59, 60–64, 65–69, ≥70 years), education (<7, 7–11, ≥12 years), occupational physical activity (light, medium, or vigorous), family history of prostate cancer (no vs yes), diabetes (never vs ever), smoking habits (never, former, current: <20, ≥20 cigarettes/day), drinking habits (never, former, current: <14, 14–20, 21–34, ≥35 drinks/week), nonalcohol energy intake (kcal continuous), body mass index (<25, 25–29, ≥30 kg/m^2), body mass index at age 30 years (<25, 25–29, ≥30 kg/m^2).

‡ The sums do not add up to the total because of missing values.

§ Values were from χ^2 tests for trend.

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Response

We are grateful for the opportunity to comment on the letter by Polesel et al. on their study on coffee and prostate cancer risk. Indeed, given the novel findings of our initial report, we recognize the important role of the research community in validating these results in additional study populations.

The authors report no evidence for an inverse association between coffee consumption and the risk of total prostate cancer or Gleason grade 7–10 disease. It is noteworthy that the odds ratios and confidence intervals reported in the correspondence are, in fact, compatible with our own results. We found only a modest inverse association for total prostate cancer risk, and for grade 8–10 cancers, we found an inverse association only in the highest category of intake with no dose-response. Moreover, although rereviewed Gleason grade is an important predictor of prostate cancer outcomes, there are inherent challenges in deriving grade information from original pathology reports. There are well-documented shifts in grading over time and across institutions (1,2), which may influence epidemiological studies that use historical Gleason data, including our own.

As the authors note, the substantially lower risk was found for lethal and advanced prostate cancer among coffee drinkers. The data on stage and outcomes represent "harder" outcomes with less misclassification. Neither these results from the Italian hospital–based case–control study nor the meta-analysis by Park et al. (3) cited in the correspondence studied lethal or advanced stage cancer separately. Because of the great heterogeneity in the biological potential of prostate cancers, and the use of prostate-specific antigen screening, we consider the study of advanced and lethal prostate cancer to be critical to our understanding of clinically relevant prostate cancer.

Although high grade confers the potential for prostate cancer to be aggressive, it is conceptually distinct from lethal cancer in that progression of a localized, high-grade tumor can theoretically be prevented. As such, high-grade disease is not a surrogate for lethal disease, and small, localized high-grade cancers may actually mark the presence of protective factors.

In response to their comments on confounding by smoking, we maintain that it will mainly be an issue for the study of lethal or advanced prostate cancer because smoking is associated with more aggressive disease but not with overall incidence (4). Also, the degree of confounding by smoking will vary between populations by the prevalence of smoking and its link with coffee intake.

We agree that more studies on mechanism are needed. However, the argument of the correspondents about insulin-like growth factor 1 does not distinguish between insulin and insulin growth factor (IGF)-1. Insulin is associated with prostate cancer progression (5), whereas total IGF-1 is not (6). In addition, insulin levels and insulin resistance are affected by coffee intake, but IGF-1 is not (7).

We hope others will examine the coffee–prostate cancer association, particularly for lethal prostate cancer. We also wonder whether the authors might have the ability to link their study data with outcome data to study prostate cancer mortality or whether they may have sufficient numbers of Gleason 8–10 cancers to look at this highest risk group.

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Notes

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