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LETTER TO THE EDITOR

Coffee consumption and risk of lung cancer: the ICARE study

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Abbreviations

ICARE	Investigation of occupational and environmental causes of respiratory cancers
CSI	Comprehensive smoking index
OR	Odds ratio
CI	Confidence interval

Coffee is one of the most widely consumed beverages and a major dietary exposure in the world. In 2007, the World Cancer Research Fund (WCRF) and the American Institute of Cancer Research (AICR) concluded in its report that for the association between lung cancer with dietary exposures such as coffee intake, the data were either of too low quality, or too inconsistent or the number of studies were too few to allow conclusions to be reached [1]. A meta-analysis (2010) of 13 studies reported significant positive association between coffee consumption and lung cancer risk [2]. However, there may still be residual confounding due to smoking.

We sought to examine the association between coffee consumption and lung cancer risk in a large French population-based case–control study, the ICARE study (Investigation of occupational and environmental causes of respiratory cancers). The large sample size of this study allowed us to assess the association by gender, smoking status and histological types of lung cancer.

The study design, study population and data collection methods of ICARE study have been described in detail elsewhere [3]. In brief, ICARE study is a large multi-centre

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population-based case–control study on lung and upper aerodigestive cancers. A total of 5,926 lung cancer cases and 4,673 controls from 10 French administrative departments were recruited between 2001 and 2007. Incident lung cancer cases were identified through French cancer registries. Case eligibility criteria included histological confirmed primary malignant tumour of the lung who were aged ≤75 years at diagnosis. Lung cancers included tumours were coded according to International Statistical Classification of Diseases-Oncology (ICD-O) 3rd edition (code C33-C34). All histological types of lung cancer were included. Controls were selected from the general population via random digital dialling and were frequency-matched to the cases by age, gender and area of residence (department). Of the 5,926 lung cancer cases recruited, 4,865 met the eligibility criteria. Among the eligible cases, 486 could not be located, 781 were deceased and 238 were too sick to be interviewed. Following these exclusions, 3,360 cases remained were contacted of which, 2,926 cases (87 %) agreed to participate. Among the 4,673 controls recruited, 5 were deceased, 230 could not be reached and 27 were too sick to be interviewed. Following these exclusions, 4,441 controls remained were contacted of which, 3,555 controls (80.6 %) agreed to participate. A total of 6,481 subjects (2,926 lung cancer cases and 3,555 controls) were included in the study. Subjects were interviewed face-to-face with standardized questionnaires by trained interviewers. The questionnaire included information about socio-demographic characteristics (age, gender, marital status, and education level and birth country), residential history, medical history and family history of cancer. Besides, detailed information was collected on tobacco (quantity, types, age at starting, and time since cessation), alcohol drinking (quantity, types, age at starting, and time since cessation), consumption of coffee, tea and soft drinks (quantity, duration, age at starting, and time since cessation), anthropometric measurements (height, weight at interview, weight at 2 years before and weight at age 30) and lifetime history of occupations held for at least 1 month (job title, description of tasks performed in that job and the company production and activities). The data collected on lifetime occupations were coded according to the International Standard Classification of Occupations (ISCO) and French Nomenclature of Activities (NAF) for industries. These coded data were translated into jobs known (list A) or suspected (list B) to be associated with lung cancer. Details have been described elsewhere [3].

If the subject was too sick, a shortened version of the questionnaire was used to interview him or her, or next-of-kin. This shortened version mainly included information on smoking, alcohol drinking and occupational history but not coffee, tea and soft drinks. Further details on questionnaires can be found elsewhere [3].

For the present analysis, we excluded the subjects who answered the short version of the questionnaire (cases = 242 and controls = 74). After the exclusion, 6,165 subjects (2,684 cases and 3,481 controls) remained for the analysis. Unconditional logistic regression models were used to estimate odds ratios (ORs) with 95 % confidence intervals (95 % CIs) for the association between coffee consumption and lung cancer risk. Coffee consumption was classified into quartiles based on the distribution among controls by excluding never consumers: quantity (<2, 2–3, 3–5, ≥5 cups/day), duration (<30, 30–40, 40–49, ≥49 years) and lifetime cumulative consumption (<62, 62–112, 112–184, ≥184 cup-years). Never coffee consumers were used as the reference category. Smoking history was combined into a comprehensive smoking index (CSI) that included mean number of cigarettes/day, duration and time since cessation [4]. Occupational history was defined as yes/no (subjects who had at least one job in the list A of occupations/subjects who had no job in the list A of occupations). Models were adjusted for age, gender, area of residence, CSI and occupational history. In analysis stratified by smoking status, never smokers were defined as subjects who reported that they had never smoked, former smokers were defined as subjects who had stopped smoking for at least 2 years before the interview and current smokers were defined as subjects who had smoked at least 100 cigarettes in their life time and reported smoking at the time of interview. Also, subjects who had smoked within 2 years of interview but stopped smoking at the time of interview were defined as current smokers. All analyses were performed using the SAS 9.3 software (SAS Institute, Cary, NC) and a p value <0.05 was considered as statistically significant.

In total of 6,165 subjects (77.8 % men and 22.2 % women), 94.8 % drank coffee and 4.7 % did not drink coffee. Odds ratios and the corresponding 95 % CIs for coffee consumption and lung cancer risk are presented in Table 1. Coffee consumption was found to be associated with an increased risk of lung cancer in the age, area of residence and gender adjusted model, however after adjustment for smoking and occupational history this association approached null and non-significant. The OR was 1.08 (95 % CI 0.80–1.47) for ever consumers, 1.07 (95 % CI 0.77–1.48) for ≥5 cups/day, 1.02 (95 % CI 0.72–1.43) for duration of consumption ≥49 years, and 1.02 (95 % CI 0.73–1.42) for lifetime cumulative consumption ≥184 cup-years compared with never consumers (Table 1). We performed separate analysis by gender and found no significant associations between coffee consumption and lung cancer risk in either men or women (Table 1). In addition, no significant associations were observed after stratifying cases by histological type. Adjusted ORs for ≥5 cups/day versus never consumers for adenocarcinoma, squamous-cell carcinoma, large-cell carcinoma and small-cell carcinoma were 1.09 (95 % CI

Table 1 Odds ratio of lung cancer according to coffee consumption, the ICARE study 2001–2007

Coffee	Men and women				Men			Women		
Consumption	Cases	Controls	OR (95% CI)[1]	OR (95% CI)[2]	Cases	Controls	OR (95% CI)[3]	Cases	Controls	OR (95% CI)[3]
Status										
Never	97	195	Reference	Reference	55	119	Reference	42	76	Reference
Ever	2562	3282	1.65 (1.28–2.12)	1.08 (0.80–1.47)	2000	2597	1.09 (0.72–1.65)	562	685	1.25 (0.79–1.97)
Missing	25	4	–	–	19	4	–	6	–	–
Quantity (cups/day)										
Never	97	195	Reference	Reference	55	119	Reference	42	76	Reference
<2	475	696	1.43 (1.09–1.88)	1.33 (0.96–1.86)	355	525	1.30 (0.83–2.04)	120	171	1.61 (0.97–2.67)
2 3	502	762	1.39 (1.06–1.82)	1.03 (0.74–1.44)	396	601	1.07 (0.69–1.67)	106	161	1.08 (0.64–1.83)
3 5	733	1045	1.50 (1.15–1.96)	0.94 (0.68–1.31)	578	844	0.95 (0.61–1.46)	155	201	1.13 (0.68–1.88)
≥5	838	773	2.37 (1.82–3.10)	1.07 (0.77–1.48)	662	622	1.11 (0.72–1.72)	176	151	1.15 (0.69–1.94)
Missing	39	10	–	–	28	9	–	11	1	–
Duration (years)										
Never	97	195	Reference	Reference	55	119	Reference	42	76	Reference
<30	430	761	1.24 (0.93–1.65)	0.97 (0.68–1.37)	280	595	0.93 (0.58-1.48)	150	166	1.25 (0.73–2.13)
30–40	730	784	1.94 (1.48–2.54)	1.17 (0.84–1.63)	568	666	1.16 (0.75–1.81)	162	118	1.47 (0.88–2.47)
40–49	694	810	1.76 (1.34–2.31)	1.12 (0.80–1.56)	576	660	1.17 (0.76–1.82)	118	150	1.09 (0.63–1.87)
≥49	656	857	1.61 (1.21–2.13)	1.02 (0.72–1.43)	537	619	1.02 (0.65–1.61)	119	238	1.05 (0.61–1.83)
Missing	77	74	–	–	58	61	–	19	13	–
Lifetime cumulative (cup–years)										
Never	97	195	Reference	Reference	55	119	Reference	42	76	Reference
<62	500	797	1.36 (1.04–1.78)	1.27 (0.91–1.77)	357	601	1.24 (0.79–1.93)	143	196	1.53 (0.93–2.52)
62–112	540	798	1.45 (1.10–1.89)	1.03 (0.74–1.44)	419	641	1.10 (0.71–1.71)	121	157	1.03 (0.61–1.73)
112–184	601	807	1.59 (1.21–2.08)	0.96 (0.69–1.34)	484	672	0.98 (0.63–1.52)	117	135	1.13 (0.67–1.92)
≥184	858	804	2.29 (1.75–2.99)	1.02 (0.73–1.42)	694	621	1.06 (0.68–1.64)	164	183	1.09 (0.64–1.83)
Missing	88	80	–		65	66	–	23	14	–

[1] Adjusted for age (≤52, 52–60, 60–67, >67), gender, area of residence (Bas Rhin, Calvados, Doubs/Territoire de Belfort, Haut Rhin, Hérault, Isère, Loire Atlantique, Manche, Somme, and Vendée)

[2] Adjusted for age (≤52, 52–60, 60–67, >67), gender, area of residence (Bas Rhin, Calvados, Doubs/Territoire de Belfort, Haut Rhin, Hérault, Isère, Loire Atlantique, Manche, Somme, and Vendée), CSI (continuous) and occupational history (yes/no)

[3] Adjusted for age (≤52, 52–60, 60–67, >67), area of residence (Bas Rhin, Calvados, Doubs/Territoire de Belfort, Haut Rhin, Hérault, Isère, Loire Atlantique, Manche, Somme, and Vendée), CSI (continuous) and occupational history (yes/no)

0.73–1.64), 1.04 (95 % CI 0.63–1.72), 1.22 (95 % CI 0.56–2.66) and 0.75 (95 % CI 0.42–1.35) respectively (data not tabulated). Similar results were observed for duration of coffee consumption and for lifetime cumulative coffee consumption (data not shown). Stratified by smoking status, no significant associations were observed among never smokers (OR 1.03, 95 % CI 0.54–1.94; for ≥5 cups/day vs. never), former smokers (OR 1.47, 95 % CI 0.80–2.70; for ≥5 cups/day vs. never) and current smokers (OR 0.77; 95 % CI 0.42–1.44; for ≥5 cups/day vs. never) (data not tabulated). We found similar results for duration of coffee consumption and for lifetime cumulative coffee consumption among never, former and current smokers (data not shown).

In this large French population-based case–control study, we found no significant association between coffee consumption and lung cancer risk. Also, no significant associations were found when stratified by histological type, gender or smoking status. In particular, we observed no significant association for consumption of 5 or more cups of coffee per day, duration of consumption of 49 years or more and life time cumulative consumption of 184 cup-years or more.

The available data on the association between coffee consumption and lung cancer risk are inconsistent. A meta-analysis (2010) by Tang et al., reported no association for coffee consumption with lung cancer in 8 case–control studies (RR 1.13; 95 % CI 0.90–1.41) and a positive association in 5 cohort studies (RR 1.57; 95 % CI 1.15–2.14) for highest versus lowest coffee consumption. Results by country, showed a positive association for studies conducted in USA and Japan and no association for studies conducted in Europe. The RRs were 1.33 (95 % CI 1.07–1.65) for the four American studies, 1.34 (95 % CI 1.05–1.70) for the 4 Japanese studies and 1.26 (95 % CI 0.76–2.09) for the 5 European studies. When all studies were combined coffee consumption showed an increased risk for lung cancer (RR 1.27; 95 % CI 1.04–1.54) [2]. In the subgroup analyses, findings of this meta-analysis indicated no significant associations by histological type of lung cancer or smoking status [2]. More recently, Yu et al. conducted a meta-analysis of cohort studies for coffee consumption with cancer risk. Results by cancer sites, showed no significant association between coffee consumption and lung cancer risk. The RR based on 5 cohort studies was 1.17 (95 % CI 0.92–1.42) for moderate versus low coffee consumption [5]. A plausible explanation for inconsistencies in studies of coffee consumption and risk of lung cancer risk may be residual confounding because of cigarette smoking, which is correlated with coffee consumption [6].

Strengths of our study include large sample size, comprehensive information on coffee consumption and potential confounders. Residual confounding by smoking is always a great concern in studies of lung cancer. In order to minimize this problem, we carefully adjusted for smoking by using CSI, as it has been shown to provide a parsimonious representation of lifetime smoking history in relation to lung cancer [4]. In addition, we were able to perform the analyses by histological types, gender and smoking status. Our study also has some limitations. First, recall bias is a possibility with regard to coffee consumption because of case–control design. Second, the association of coffee consumption with lung cancer is not commonly known, hence non-differential bias among cases and controls cannot be ruled out, which may have biased our estimates towards the null. However, recall of coffee consumption has been shown satisfactorily reproducible and valid [7]. In addition, a previous analysis in the ICARE population showed a non-significant inverse association between coffee consumption and oral cavity cancer risk [8]. Lastly, we lacked information on types and preparation methods of coffee consumed. Any potentially cancer-related bioactive components such as caffeine, polyphenol and diterpenes [9] may differ according to the type and preparation method of coffee consumed [10].

From this study, it appears that the association between coffee consumption and lung cancer risk is strongly confounded by smoking, where a significant OR of 1.65 (95 % CI 1.28–2.12) adjusted for age, gender and area of residence comparing ever consumers vs never consumers was substantially reduced to 1.09 (95 % CI 0.80–1.49) after additional adjustment for only smoking.

In conclusion, findings of this French population-based case–control study suggest that coffee consumption is not associated to the risk of lung cancer. Furthermore, this study shows that smoking strongly confound the association between coffee consumption and lung cancer risk.

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Conflict of interest None.

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