RESEARCH ARTICLE

Lack of Association between Fingernail Selenium and Thyroid Cancer Risk: A Case-Control Study in French Polynesia

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Abstract

Background: Numerous studies have suggested that selenium deficiency may be associated with an increased risk for several types of cancer, but few have focused on thyroid cancer. Materials and Methods: We examined the association between post-diagnostic fingernail selenium levels and differentiated thyroid cancer risk in a French Polynesian matched case-control study. Conditional logistic regression models were used to estimate odds ratios and 95% confidence intervals. Results: The median selenium concentration among controls was 0.76 μg/g. Significantly, we found no association between fingernail selenium levels and thyroid cancer risk after conditioning on year of birth and sex and additionally adjusting for date of birth (highest versus lowest quartile: odds-ratio=1.12, 95% confidence interval: 0.66-1.90; p-trend=0.30). After additional adjustment for other covariates, this association remained non-significant (p-trend=0.60). When restricting the analysis to thyroid cancer of 10 mm or more, selenium in nails was non-significantly positively linked to thyroid cancer risk (p-trend=0.09). Although no significant interaction was evidenced between iodine in nails and selenium in nails effect (p=0.70), a non-significant (p-trend=0.10) positive association between selenium and thyroid cancer risk was seen in patients with less than 3 ppm of iodine in nails. The highest fingernail selenium concentration in French Polynesia was in the Marquises Islands (M=0.87 μg/g) and in the Tuamotu-Gambier Archipelago (M=0.86 μg/g). Conclusions: Our results do not support, among individuals with sufficient levels of selenium, that greater long-term exposure to selenium may reduce thyroid cancer risk. Because these findings are based on post-diagnostic measures, studies with prediagnostic selenium are needed for corroboration.

Keywords: Thyroid cancer - selenium - diet - fingernail - case-control study

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Introduction

Thyroid cancer, the most common malignancy of the endocrine system, accounts for less than 2% of all cancers diagnosed worldwide (Ron and Schneider, 2006). Iodine and selenium are dietary factors for which there is the most information to play a role in the risk of differentiated thyroid cancer. Moreover, these elements and the family of molecules in which they are present (thyroid hormones, isothiocyanates, selenoproteins) are substrates of enzymes encoded by genes whose polymorphisms are most suspected to play a role in the risk of thyroid cancer: FOXE1, FOXE2 for iodine (Gudmundsson et al., 2009), and genetic family of Glutathione-S-transferases for selenium (Adjadj et al., 2009).

Selenium is an essential trace element present mainly in grains, meat, fish, eggs, and dairy products, as well as multivitamin supplements (Aseth et al., 1990; Jung and Seo, 2010). Like iodine, the selenium content of a given food strongly depends upon the geographic location where it is produced, as plant uptake is largely influenced by the availability and chemical species of selenium in the soil (Aseth et al., 1990). The redox-protective properties of selenium are important during oxidative thyroid hormone production, in which thyroid cells produce excess H₂O₂ and reactive oxygen species. Due to its ability to...
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to each case by date of birth (±3 months for the first
to the birth registry in French Polynesia and matched
For each case, two controls were randomly selected
were not interviewed because they had died (n=14), could
were not interviewed because they had died (n=16). After
these exclusions, 35 cases had one and 25 cases had no
matched controls. Each of the 25 cases with no matched
control was then matched to a control from among cases
that had two matched controls; the matching criteria for
date of birth were relaxed if necessary.

In total, the study population included 229 interviewed
cases and 373 interviewed controls, with 85 cases (37%)
matched to one control and 144 cases (63%) matched to
two controls. We further excluded 6 cases and 9 controls
for missing data on fingernail selenium, and a batch of
8 cases and 33 controls for which all measures of any
elements in the fingernails were returned as null. The final
analytic population was 215 cases and 331 controls.

The French Polynesian Ethics Committee approved
the study, and written informed consent to participate in
the study and to contact his or her physician was obtained
from each participant.

Detailed characteristics of cases and controls are, as
well as thyroid cancer risk factor estimates are reported
elsewhere (De Vathaire et al. 2010, Xhaard et al., 2014).

Data collection
Home addresses for cases and controls were obtained
through the territorial medical insurance plan that offers
coverage for all inhabitants. In-person interviews were
conducted in the participants’ homes (though some
cases were interviewed at the hospital on the day of their
usual follow-up consultation) by trained interviewers
and medical staff using a structured questionnaire
which included questions regarding ethnicity, education,
smoking, weight at various ages, personal history
of thyroid disease and cancer, places of residence,
reproductive and hormonal exposures, history of medical
X-rays and diet.

We used a French food composition table (Favier
et al., 1995) for the calculation of iodine and selenium
intake because data were lacking in the Pacific Islands
food composition tables (Dignan et al., 2004). The
overall iodine intake took into account all foods of the
questionnaire, except iodized salt because we had no
information on the amount of iodized salt consumption.
All participants provided fingernail clippings on the
date of the interview. Clippings were stored in paper
envelopes at room temperature before being transferred
to the toxicology centre of the Institut National de Sante
Publique du Quebec (INSPQ).

Fingernail selenium and iodine measurements
Nail samples were digested under basic conditions
using trimethylammonium hydroxide for iodine and
under acidic conditions with nitric acid for selenium.
The digested material was directly analysed by ICP-MS
(inductively coupled plasma mass spectrometry, Perkin
Elmer Sciex, Elan DRCII with autosampler ESI SC-4 and
work station Elan version 3.0) (Elwaer and Hintelmann,
Statistical analysis

Descriptive statistics and trend tests in univariate analysis were performed using non-parametric Jonckheere-Terpstra test for association between two quantitative variables; non-parametric Wilcoxon rank test for association between a qualitative variable with two classes and a quantitative variable; and non-parametric Kruskal-Wallis rank tests for association between a qualitative variable with more than two classes and a quantitative variable.

The association between selenium in nails and other parameters has been investigated using generalized linear models.

We used conditional logistic regression to estimate OR and 95% CI for thyroid cancer by fingernail selenium concentration. Selenium was categorized into quartiles based on the distribution among the controls. All models were conditioned on year of birth (<1945, 1945-1955, 1955-1965, ≥1965) and sex to control for residual confounding by age. Multivariable models were additionally adjusted for ethnicity (Polynesian, mixed, other), education (primary school or lower vs. middle school or higher), BMI at the moment of cancer (<25, 25-29.9, ≥30 kg/m², missing), current smoking (yes vs. no), and radiotherapy treatment to head or neck (ever vs. never). These associations were also evaluated by sex, smoking status, BMI, thyroid cancer histology, tumour size, fingernail iodine and dietary iodine. Effect modification of selenium levels by sex, smoking status, BMI, thyroid cancer histology, tumour size, fingernail iodine and dietary iodine was evaluated using the likelihood ratio test comparing a model with an interaction term to one without. We also investigated for potential bias due to the delay between thyroid cancer diagnosis and fingernails sampling, by performing separate analysis for various categories of delay.

All statistical analyses were conducted using SAS software (version 9.3, SAS Institute Inc., Cary, NC, USA).

Results

The cases and controls were generally comparable in terms of ethnicity and level of education. Thirty percent of the tumours were less than 10 mm. About 70% of cases had papillary thyroid cancer, and 30% had a follicular type.

Among controls, higher fingernail selenium levels were observed in older people (p<0.001), and people who have higher BMI (p=0.001) and in non-smokers (p<0.0001), but in a multivariate analysis, only age (p=0.01) and smoking (p<0.0001) remained significant (Table 1). The highest fingernail selenium levels were in inhabitants of the Marqueses Islands (M=0.87 μg/g) and of the Tuamotu-Gambier Archipelago (M=0.86 μg/g) (Figure 1). Adjusting by other factors, including estimated selenium and iodine in diet, selenium in the fingernails of controls from the Tuamotu-Gambier Archipelago remained significantly higher than in the rest of French Polynesia.
Polynesian, but not from the Marquises Islands (Table 1). On the contrary, among cases, only selenium in fingernails of the Marquises Islands inhabitants remained higher than in the other inhabitants of French Polynesia (p=0.05) (Table 1).

We did not evidence a significant association between fingernail selenium levels and thyroid cancer risk in models that were conditioned on year of birth and gender and further adjusted for year of birth (highest versus lowest quartile: OR=1.12, 95%CI: 0.66-1.90; p-trend=0.30) (Table 2). After additional adjustment for age at the moment of the diagnosis of cancer, ethnicity, education, BMI, smoking status and radiotherapy treatment to the head or neck, this association with the risk of thyroid cancer comparing the highest to the lowest quartile was also non-significant (OR=1.02, 95%CI: 0.56-1.84; p-trend=0.60) (Table 2).

Among the studied population, average fingernail selenium concentration was 0.75 µg/g in smokers and 0.80 µg/g in non-smokers (p=0.0001). We did not observe evidence for a significant effect modification by sex, smoking status, BMI, histological type, fingernail iodine and dietary iodine (all p-interaction>0.05; Table 2). A significant interaction was evidenced between selenium and tumour size (p=0.04); when restricting the analysis to differentiated thyroid cancer of 10 mm or more, selenium in nails was nearly significantly positively (p=0.09) linked to thyroid cancer risk. Although no significant interaction

### Table 1. Predictor of Selenium Concentration in Fingernails in Thyroid Cancer Patients and Controls

<table>
<thead>
<tr>
<th>Cases</th>
<th>Regression Coefficient (SD†)</th>
<th>p-value*</th>
<th>Controls</th>
<th>Regression Coefficient (SD†)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dietary selenium (mg/1,000 kcal)</strong></td>
<td>&lt;0.001 (&lt;0.001)</td>
<td>0.60</td>
<td><strong>Dietary iodine (mg/1,000 kcal)</strong></td>
<td>&lt;0.0002 (&lt;0.0001)</td>
<td>0.06</td>
</tr>
<tr>
<td>Gender (women/men)</td>
<td>-0.01 (0.03)</td>
<td>0.80</td>
<td></td>
<td>0.04 (0.02)</td>
<td>0.06</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.0002 (0.0001)</td>
<td>0.30</td>
<td></td>
<td>0.0001 (0.0001)</td>
<td>0.20</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.0026 (0.0002)</td>
<td>0.03</td>
<td></td>
<td>0.0002 (0.0001)</td>
<td>0.01</td>
</tr>
<tr>
<td>Currently smoking (yes/no)</td>
<td>-0.06 (0.02)</td>
<td>0.01</td>
<td></td>
<td>-0.06 (0.01)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Marquises Islands (yes/no)</td>
<td>0.14 (0.07)</td>
<td>0.05</td>
<td></td>
<td>0.04 (0.06)</td>
<td>0.40</td>
</tr>
<tr>
<td>Tuamotu-Gambier Archipelago (yes/no)</td>
<td>0.06 (0.04)</td>
<td>0.10</td>
<td></td>
<td>0.12 (0.03)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

*Standard deviation; †Regression coefficient t-test

### Table 2. Fingernail Selenium and Thyroid Cancer by Various Confounding Factors in French Polynesia, 1981-2003

<table>
<thead>
<tr>
<th>Quartiles of selenium (µg/g)</th>
<th>Q1 (0.00-0.68)</th>
<th>Q2 (0.68-0.76)</th>
<th>Q3 (0.76-0.86)</th>
<th>Q4 (0.86-1.30)</th>
<th>p-trend*</th>
<th>p-interaction**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Cases/controls</td>
<td>51/93</td>
<td>56/81</td>
<td>50/79</td>
<td>58/78</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 1</td>
<td>1.00</td>
<td>1.16 (0.70-1.94)</td>
<td>1.06 (0.64-1.77)</td>
<td>1.12 (0.66-1.90)</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.08 (0.62-1.90)</td>
<td>1.10 (0.62-1.96)</td>
<td>1.02 (0.56-1.84)</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>2/15</td>
<td>8/9</td>
<td>6/5</td>
<td>7/11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>?†</td>
<td>?†</td>
<td>752.6 (&lt;0.001 -&gt; ?†)</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>0.91 (0.38-2.18)</td>
<td>1.02 (0.45-2.32)</td>
<td>1.07 (0.47-2.46)</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>0.95 (0.53-1.71)</td>
<td>0.95 (0.51-1.74)</td>
<td>0.90 (0.48-1.70)</td>
<td>0.90</td>
<td>0.20</td>
</tr>
<tr>
<td>Current smoker</td>
<td>36/60</td>
<td>36/41</td>
<td>23/32</td>
<td>26/29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.29 (0.68-2.43)</td>
<td>1.08 (0.53-2.19)</td>
<td>1.19 (0.59-2.41)</td>
<td>0.40</td>
<td>0.70</td>
</tr>
<tr>
<td>BMI &lt;30 kg/m²</td>
<td>35/68</td>
<td>27/52</td>
<td>23/53</td>
<td>24/48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>0.95 (0.49-1.84)</td>
<td>0.81 (0.41-1.62)</td>
<td>0.76 (0.37-1.55)</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>BMI ≥30 kg/m²</td>
<td>16/25</td>
<td>28/28</td>
<td>27/26</td>
<td>34/30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.65 (0.70-3.90)</td>
<td>1.74 (0.73-4.18)</td>
<td>1.97 (0.83-4.66)</td>
<td>0.15</td>
<td>0.30</td>
</tr>
<tr>
<td>Papillary Cases/controls</td>
<td>40/58</td>
<td>39/56</td>
<td>37/66</td>
<td>49/56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>0.95 (0.52-1.76)</td>
<td>0.81 (0.44-1.49)</td>
<td>1.18 (0.64-2.18)</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.74 (0.59-5.08)</td>
<td>3.79 (1.12-12.8)</td>
<td>0.99 (0.29-3.29)</td>
<td>0.80</td>
<td>0.60</td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.84 (0.59-5.75)</td>
<td>1.79 (0.61-5.29)</td>
<td>1.84 (0.59-5.75)</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>Tumours &lt;10 mm</td>
<td>32/59</td>
<td>30/49</td>
<td>28/43</td>
<td>33/39</td>
<td>0.17</td>
<td>0.22</td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.04 (0.53-2.02)</td>
<td>1.19 (0.60-2.36)</td>
<td>1.37 (0.69-2.72)</td>
<td>0.09</td>
<td>0.04</td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>0.98 (0.46-2.09)</td>
<td>1.18 (0.56-2.49)</td>
<td>1.44 (0.66-3.11)</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Fingernail iodine &lt;3 ppm</td>
<td>27/44</td>
<td>33/38</td>
<td>31/39</td>
<td>23/44</td>
<td>0.10</td>
<td>0.07</td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>0.83 (0.41-1.70)</td>
<td>0.95 (0.44-2.06)</td>
<td>1.40 (0.67-2.95)</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.15 (0.56-2.37)</td>
<td>1.13 (0.52-2.47)</td>
<td>0.99 (0.47-2.06)</td>
<td>0.90</td>
<td>0.70</td>
</tr>
<tr>
<td>OR (95% CI) 2, 3</td>
<td>1.00</td>
<td>1.71 (0.80-3.64)</td>
<td>1.31 (0.63-2.72)</td>
<td>0.94 (0.43-2.06)</td>
<td>0.90</td>
<td>0.50</td>
</tr>
</tbody>
</table>

*Calculated using the Wald test for selenium modelled as a continuous variable (per quartile); **Calculated using the likelihood ratio test comparing a model with an interaction term to one without; †Not estimable; 1Adjusted for year of birth (continuous); 2Adjusted for year of birth (continuous), age at the moment of the diagnosis of cancer (continuous), gender, ethnicity, education, BMI, smoking status, radiotherapy treatment to head or neck; 3One case and one control were excluded from the analysis due to missing data on BMI.
was evidenced between iodine in nails and selenium in nails effect (p=0.70), a nearly significant positive association (p=0.10) between selenium and thyroid cancer risk was seen in patients with less than 3 ppm of iodine in nails. A similar result also has been found in which a nearly significant positive association (p=0.10) between selenium and thyroid cancer risk was seen in patients with less than 117 mg/1,000 kcal of dietary iodine (Table 2).

There was no clear association of fingernail selenium for cases who were interviewed and provided fingernail samples less than 3 years, 3 to 7, 7 to 11 or more than 11 years after diagnosis (all p-trend >0.05; Table 3).

### Discussion

Our objective was to examine the association between fingernail selenium concentrations and thyroid cancer in French Polynesia, a country highly exposed to selenium mainly through fish consumption and characterized by mild iodine deficiency (Clero et al., 2012).

Overall, we did not evidence a significant association between fingernail selenium levels and thyroid cancer risk. Fingernail selenium levels were higher in subjects with high BMI and in non-smokers, and among controls only, in older subjects. Furthermore, fingernail selenium levels were higher in inhabitants of the Marquesas Islands and the Tuamotu-Gambier Archipelago. Selenium in nails was nearly significantly positively linked to the risk of thyroid cancer of 10 mm or more (p=0.09). Lastly, a nearly significant positive association (p=0.10) between selenium and thyroid cancer risk was seen in patients with less than 3 ppm of iodine in nails.

This analysis has important strengths including, the population-based design with virtually exhaustive identification of thyroid cancer cases in isolated Pacific Islands and a high participation rate among cases and population control subjects, which were from the population register of French Polynesia (Brindel et al., 2009). Another important strength is that French Polynesia ranks as one of world’s leading consumers of fish (Dewailly et al., 2008), a major dietary source of selenium (Dewailly et al., 2008), which increased the power of our analysis. Furthermore, despite recent changes in lifestyle and nutrition, an important proportion of inhabitants (at least the ones living outside Tahiti), still have a traditional diet of fish, starchy roots and fruits, and consumed at the time of interview few imported foods that are high in fat and low in fibre (World Health Organization, 2003), and thus are more likely to accurately report their dietary intake.

This analysis also has some limitations. In regard to the statistical method, when we conditioned on age and sex using the original matching criteria (year of birth, months and sex), we observed similar results but reduced statistical power since matched groups that were missing either a case or control were dropped from the analysis.

Because of the transition in diet habits from a traditional Polynesian diet to a more Westernized one, the results of this case-control study about diet in adulthood could be confounded by diet in previous periods.

We did not find a correlation between selenium measured in fingernails and dietary selenium intake, as estimated using dietary questionnaire data and a French food composition. This lack of correlation was not surprising because the concentration of selenium in foods is largely variable and its quantification from food composition table data is uncertain. Indeed, its concentration in vegetables is dependent on the soil content in a particular geographical location (Asesset al., 1990), and its concentration in fishes is dependent on the type of cooking and variable between species (Favier et al., 1995). Therefore, our estimation of selenium in diet is probably uncertain. Thus, biomarker measures are essential in investigating the relationship between selenium exposure and chronic disease risk.

Selenium concentration in nails is a highly reproducible value. In a cohort on the investigation of dietary supplement use and cancer risk in Western Washington state, the concentration of toenail selenium without selenium supplement was about six times higher than the concentration of plasma selenium without selenium supplement, mean toenail and plasma concentrations were 1.02±0.21 µg/g and 161±29 µg/L, respectively (Sativa et al., 2006). There are advantages to measure selenium concentration in fingernails rather than blood: the quantity of selenium in nails is more stable, cumulative, and integrates exposure occurring from 12 to 18 months before sampling (Fleckman, 1985). Additionally, collecting, transporting and storing fingernails are easier than blood.

A previous cross-sectional study, including 195 adults aged 18 years old and over from Tahiti and the Moorea islands, found that serum selenium levels in French Polynesia in 2008 were similar to those observed in Inuit adults in 1992; however, these are four times lower than France (foods imported to Polynesia come from France), even considering the whole blood/plasma ratio (Dewailly et al., 2008).

We found that the highest fingernail selenium concentrations of French Polynesia were in the Marquesas Islands and in the Tuamotu-Gambier Archipelago, which is similar to observations performed on cord blood selenium concentrations...
concentration in French Polynesian new-borns in 2008 (Dewailly et al., 2008). These highest values are probably mostly attributable to higher seafood consumption, but the results shown in Table 1, in which the higher fingernail selenium values in controls living in the Tuamotu-Gambier Archipelago remains when adjusting for estimated dietary selenium intake, showing that other factors could interact, or that selenium level could be higher in the Tuamotu-Gambier Archipelago fishes. Because most of the fishes eaten in the atolls of the Tuamotu-Gambier Archipelago come from the lagoon, rather than the open sea like other archipelagos of French Polynesia, this result could be due to an under-estimation of selenium contents for lagoon fishes in food composition tables.

Among the studied population, fingernail selenium concentration averages in French Polynesian, 0.75 ppm in smokers and 0.80 ppm in non-smokers (p<0.0001), are very similar to those measured in other studies, and in particular in a large cohort study of US women, which have shown that toenail selenium was significantly reduced among cigarette smokers (M=0.75, SD=0.12, among 146 current smokers; and M=0.82, SD=0.16, among 311 never smokers; p<0.001) (Hunter et al., 1990).

We found a positive relationship between BMI and selenium in fingernails, both in cases and controls (Table 1). Our result is in opposition with most European surveys (Arnaud et al., 2006; Meplan et al., 2007; Ortega et al., 2012) or US populations (Bleys et al., 2009), in which obese patients have lower serum selenium concentration, but in agreement with Dewailly’s survey of a French Polynesian sampling in which selenium concentration in blood was positively linked to BMI (Dewailly et al., 2008), the regression coefficient (β) being 0.02, i.e. ten times higher than in our study, among the controls (β=0.002). A possible explication is that in the general population, BMI has a trend to rise with age, if we do not consider extreme ages. Furthermore, older people have more possibilities to eat traditional food, which is rich in selenium.

There may be a range of selenium that offers optimal protection against cancer development in general, as a deficiency in selenium has been associated with an increased risk of cancer, this association having been evidenced for selenium in hair and nails and prostate cancer in Malaysia (Karimi et al., 2012), and selenium in serum and, respectively bladder carcinoma in China (Guo et al., 2012), and breast cancer in India (Singh et al., 2005). In the latter case-control study, it has been estimated that each increase of one μmol/l of selenium was associated to decrease in 7% of breast cancer risk (Singh et al., 2005). Nevertheless, selenium supplementation may reduce cancer risk only in selenium-deficient individuals.

Few studies have examined the association between selenium and thyroid cancer risk, however, we haven’t found association between fingernail selenium and thyroid cancer risk in our results. In a case-control study of 43 cases and 129 matched controls in Norway, prediagnostic serum selenium levels were inversely associated with thyroid cancer; levels ≥1.25 and 1.26-1.64 μmol/l were associated with a 7.70- and 6.10-fold increased risk of thyroid cancer compared to levels ≥1.65 μmol/l (Glattre et al., 1989). This case-control study also showed, when considering the delay from blood sampling to diagnosis of the case, that the protective effect of high serum selenium concentrations was restricted to the seven-year period prior to the diagnosis of thyroid cancer, because the serum selenium concentration of cases tended to decrease, relatively to controls, when the delay from blood sampling to the diagnosis was shorter. Similarly, in an Austrian survey the average selenium blood concentration was 1.14 μmol/l in 554 healthy controls, 0.97 μmol/l in 42 patients with follicular thyroid carcinoma and 1.02 μmol/l in 73 patients with papillary thyroid carcinoma (Moncayo et al., 2008).

Our study did not evidence a significant association between fingernail selenium levels and thyroid cancer, even when considering only patients for which the delay between cancer diagnosis and nails sample was less than seven or less than three years (Table 3). It has to be noted that over a period of six years, selenium in toenails was one of the most reproducible trace elements (Garland et al., 1993). Therefore, our non-significant results are probably not due to the fact that we investigated post-diagnosis selenium levels rather than prediagnosis ones, except if thyroid cancer, by itself, modifies selenium level in nails. A possible explication for the lack of association could be the iodine status of French Polynesians, who could be less frequently iodine deficient than Norwegians because selenium acts synergistically with iodine. These results could nevertheless also be due to the fact that fingernail samplings among cases were performed after thyroid cancer diagnosis and therefore during thyroid hormone substitution treatment, such as levothyrox, which could interact with selenium. Indeed, all three mono-deiodinase enzymes are selenium-dependent and are involved in thyroid hormone regulation. In this way, selenium status may affect both thyroid hormone homeostasis and iodine availability (Cann et al., 2000; Brauer et al., 2006; Köhrle and Gärtner, 2009). Lastly, we evidenced a nearly significant positive association (p=0.15) between fingernail selenium and thyroid cancer risk in patients with more than 30 kg/m² BMI (Table 2). This result has to be considered with caution because it is nearly significant, but it could be due to some specificity of obese patients.

Because cigarette smoking has been shown to be inversely associated with both selenium status (Lloyd et al., 1983) and thyroid cancer risk (Meinhold et al., 2010), it was important to adequately control for these exposures in our analysis. Despite having evidenced a lower selenium status in smokers than in non-smokers, we failed to show an interaction between fingernail selenium levels, smoking habit and thyroid cancer risk: both in smokers and non-smokers, selenium status did not influence thyroid cancer risk. Nevertheless, it should be noted that such interaction tests are not very powerful in our study, given the number of patients.

In summary, our results do not support, among individuals with sufficient levels of selenium, that greater long-term exposure to selenium may reduce thyroid cancer risk. Because these findings are based on post-diagnostic measures, studies with prediagnostic selenium are needed for corroboration.
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