Cancer Causes Control (2010) 21:1183–1192
DOI 10.1007/s10552-010-9545-2

ORIGINAL PAPER

Role of dietary iodine and cruciferous vegetables in thyroid cancer: a countrywide case–control study in New Caledonia

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Received: 15 July 2009 / Accepted: 17 March 2010 / Published online: 2 April 2010

Abstract Exceptionally high incidence rates of thyroid cancer have been reported in New Caledonia, particularly in Melanesian women. To clarify the reasons of this elevated incidence, we conducted a countrywide population-based case–control study in the multiethnic population of Caledonian women. The study included 293 cases of thyroid cancer and 354 population controls. Based on a food frequency questionnaire, we investigated the role in thyroid cancer of food items rich in iodine—such as seafood—and of vegetables containing goitrogens—such as cruciferous vegetables. A measure of total daily iodine intake based on a food composition table was also used. Our findings provided little support for an association between thyroid cancer and consumption of fish and seafood. We found that high consumption of cruciferous vegetables was associated with thyroid cancer among women with low iodine intake (OR = 1.86; 95% CI: 1.01–3.43 for iodine intake <96 μg/day). The high consumption of cruciferous vegetables among Melanesian women, a group with mild iodine deficiency, may contribute to explain the exceptionally high incidence of thyroid cancer in this group.

Keywords Case–control study · Diet · Iodine · New Caledonia · Thyroid neoplasms

Abbreviations

CI Confidence intervals
OR Odds ratio
TSH Thyroid stimulating hormone

Introduction

The incidence of thyroid cancer is elevated in South Pacific, particularly in New Caledonia [1], a French overseas territory of approximately 200,000 inhabitants including native Melanesians (44%), Europeans (34%), and other ethnic groups (22%) of Polynesian or Asian origin [2]. In a previous paper, we reported very high annual incidence rates for all ethnic groups in the period 1985–1999, particularly in Melanesian women (71.4/100,000) and men (10.4/100,000) [1]. As in other countries around the world, a sharp increase in incidence was observed in New Caledonia after the introduction of improved techniques of thyroid cancer screening in 1995, but the background incidence of thyroid cancer has been exceptionally elevated in this population since at least 1985 [3]. Exposure to ionizing radiations during childhood is the only well-established risk factor for thyroid cancer. Unlike French Polynesia, it should be pointed out that no nuclear test was conducted in New Caledonia, making unclear the causes of this elevated incidence. In order to identify new risk factors for thyroid cancer, we conducted a countrywide population-based

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case–control study of thyroid cancer in New Caledonia. In previous papers [4, 5], we reported that high parity and obesity may be partly responsible for the high incidence among Melanesian women. In the present paper, we examine the role of dietary factors that interfere with thyroid function, such as food with high iodine concentration and vegetables containing goitrogenic substances.

Rat experiments have shown that both iodine-rich and iodine-deficient diet induce thyroid follicular tumorigenesis, possibly through promoting effects of thyreostimulin (TSH) [6, 7]. It has been suggested that the increased incidence of thyroid papillary carcinoma observed in many countries during the last decades may be related to the introduction of iodine prophylaxis, mainly through salt iodization. However, the increasing incidence could also be attributed to the improvement of screening procedures that have led to enhanced detection of occult papillary carcinomas during the same period [1, 8, 9]. Only two epidemiological studies have investigated the role of iodine intake in thyroid cancer and reported a positive association in Hawaii [10] and an inverse association in the San Francisco Bay area [11].

Cruciferous vegetables contain thioglucosides that are metabolized to thiocyanates. These compounds inhibit iodine transport and the incorporation of iodide into thyroglobulin, thus increasing TSH secretion and thyroid cells proliferation. In animal experiments, it has been found that these substances induce thyroid carcinomas [12]. Another group of potent goitrogens are contained in food such as cassava or sweet potatoes, with high content of cyanogenic glycosides [13]. In epidemiological studies, no clear association between thyroid cancer and cruciferous vegetables or other food items containing goitrogens has been demonstrated [10, 14, 15].

In the present study, we focused on food items known to be rich in iodine such as fish, seafood, milk and dairy products, and on total dietary intake of iodine. We also studied the role of cruciferous vegetables, starchy food, and cassava containing goitrogenic substances. A possible interaction between iodine deficiency and high consumption of cruciferous vegetables was examined, as both variables decrease the iodine absorption by the thyroid gland and may enhance thyroid stimulation by the TSH. All the analyses were restricted to women, since the group of men was too small for meaningful analyses.

Material and methods

Case selection

The cases eligible to the study were patients with papillary or follicular thyroid carcinoma diagnosed between 1 January 1993 and 31 December 1999, who had been living in New Caledonia for at least 5 years at the time of cancer diagnosis.

The cases were identified from the pathology records of the two histopathology laboratories of New Caledonia, one public and one private. The ascertainment of cases was completed by searches in medical records of the main hospitals, and in the Cancer Registry of New Caledonia that also records cancer diagnoses from medical facilities throughout the country. All the pathology reports, and if not sufficient, the original histological slides, were reviewed in order to confirm the histological diagnosis and to determine the number and size of the cancerous nodules.

Cases were recruited at the beginning of the data collection in 1998, retrospectively for those diagnosed between 1993 and 1997, and prospectively for those diagnosed in 1998 and 1999. The good prognosis of papillary and follicular thyroid cancer enabled to contact most cases several years after diagnosis. Of 324 eligible cases of thyroid cancer in women, 31 could not be interviewed because the subject had died ($n = 18$), refused to participate ($n = 8$), could not be contacted ($n = 4$), or was too ill to answer ($n = 1$). Finally, 293 cases of thyroid cancer in women (response rate 90%) were included in the study, of whom 255 were papillary and 38 were follicular carcinomas.

Control selection

Controls were selected from electoral rolls recently updated at the time of study initiation in 1998 that included all New Caledonia residents aged 18 years or older. Seven groups of controls were constituted, each corresponding to a group of cases with a given year of diagnosis of the study period (1993–1999). Each control group was formed from a random selection of women in the electoral rolls in order to frequency-match the corresponding group of cases by 5-year age group. Controls were allocated a year of reference equal to the year of diagnosis of the case group for which they were selected. To be eligible, a control should have been living in New Caledonia for at least 5 years at the year of reference and should not have had a thyroid cancer before that date.

Of 405 eligible control women, 51 were not interviewed because they were dead at the time of the interview ($n = 11$), refused to participate ($n = 19$), could not be contacted ($n = 18$), were too ill to answer ($n = 2$) or for another reason ($n = 1$). Finally, 354 controls in women (response rate 87%) were included in the analysis.

Data collection

In-person interviews were conducted by trained interviewers at the subject's home using a structured questionnaire. We collected data on sociodemographic characteristics, diet, alcohol consumption, tobacco smoking, anthropometric factors, hormonal and reproductive factors, previous medical conditions, medical X-ray exposure, residential history, and family history of cancer or benign thyroid conditions. Only exposures or events which occurred before the year of diagnosis for the cases or the year of reference for the controls were taken into account.

We used a food frequency questionnaire including 110 items to assess the dietary habits during the previous 5-year period. The frequency of fruits and vegetables consumption was corrected to take the seasonality into account. Portion size was determined using color photographs representing each item in three commonly eaten amounts. Information on seasonality and weight of local fruits and vegetables was determined with a local nutritionist. The daily consumption of a food item was then estimated in grams. The 110 food items were grouped into 25 food groups. In the present paper, the following food groups were analyzed: salt water fish, brackish water fish, seafood, dairy products, cruciferous vegetables, and starchy foods.

Total energy intake (kilo-calories/day) was estimated using food composition tables developed for France [16] and for the Pacific Islands [17]. Iodine intake was computed using a French food composition table [18], which includes information on iodine content for most food items in France, but not for some local New Caledonia seafood such as giant clam, coconut crab, mangrove crab, and freshwater prawn. These food items were omitted because their consumption was negligible when compared to more common fishes and seafood.

Statistical analysis

The odds ratios (OR) and their 95% confidence intervals (CI) were calculated by unconditional logistic regression, using SAS version 9. Food items consumptions were divided into tertiles on the basis of the distribution among controls for each ethnic group. Odds ratios were adjusted for age (5-year age groups), energy intake, and ethnic group. Because the dietary profile depended on the ethnic origin, analyses were also conducted separately for the two main ethnic groups (European, Melanesian). All analyses conducted separately among Melanesian women were adjusted for the Province of residence (North, South, Loyalty Islands). Food items consumption and iodine intake were categorized into tertiles on the basis of the distribution among controls. If more than 33% of the controls declared that they never consumed a given food item, we used nonconsumers as the reference category, and we divided consumers into two classes using the median of the distribution among controls. Tests for trend were calculated by fitting a model where the median value of each class was used as a quantitative variable. Multivariate models were used to take into account potential confounding from risk factors associated with thyroid cancer risk in our data (ever had a miscarriage, irregular menstruations, number of full-term pregnancies, body mass index) [4, 5]. As the results were unchanged, odds ratios adjusted for these variables are not shown.

Results

The sociodemographic characteristics of the cases and the controls are shown in Table 1. Because of the frequency-matched design of the study, the distribution by age was similar in the two groups (chi-square test: $p = 0.66$). Proportionally more cases than controls were of Melanesian origin, and among Melanesian women more cases than controls were living in the Loyalty Islands. No statistically significant difference between cases and controls was observed with respect to educational level after adjustment for age and ethnicity.

Table 2 shows the mean values of body mass index, daily energy intake, iodine intake, and intake of selected food groups among control women, according to ethnicity and Province for Melanesian women. The mean dietary intakes differed markedly between European women and Melanesian women, particularly those from the Northern Province and the Loyalty Islands. The dietary profile of Melanesian women from the Southern Province was intermediate between that of European women (most of them living in the South) and Melanesian women in other areas. Other ethnic group women generally had food intakes close to that of the European women. As an example of specific dietary habits, it can be pointed out that brackish water fish was almost exclusively consumed by Melanesian women from the North. Milk and dairy products were consumed in greater amounts by European and other ethnic group women than by Melanesians. The Melanesian women in the Northern Province and in the Loyalty Islands had higher consumptions of cruciferous vegetables and starchy food and lower iodine intake than the other groups of women. The types of cruciferous vegetables also differed between ethnic groups.

Table 3 presents the odds ratios for food items rich in iodine (fish, seafood, dairy products) or in goitrogenic compounds (cruciferous vegetables, starchy food). No food item rich in iodine was noticeably associated with thyroid cancer, with the exception of brackish water fish that was inversely related to the disease in Melanesian women (p-trend $= 0.01$). The odds ratios for total iodine intake in the second and third tertiles were slightly above unity in Melanesian women, but were below one in European women. For cruciferous vegetables, the odds ratio in the

Table 1 Sociodemographic characteristics of thyroid cancer cases and controls—New Caledonia, 1993–1999

	Cases ($n = 293$)		Controls ($n = 354$)		OR	95% CI
	n	%	*n*	%		
Age (years)						
< 25	10	3.4	13	3.7		
25–29	24	8.2	24	6.8		
30–34	34	11.6	42	11.9		
35–39	32	10.9	38	10.7		
40–44	29	9.9	37	10.5		
45–49	36	12.3	32	9.0		
50–54	30	10.2	41	11.6		
55–59	40	13.7	37	10.5		
60–64	24	8.2	44	12.4		
65–69	18	6.1	19	5.4		
≥ 70	16	5.5	27	7.6		
Ethnic group[a]						
Melanesian	220	75.1	169	47.7	4.30	2.74, 6.75
European	32	10.9	110	31.1	1.00	Referent
Other	41	14.0	75	21.2	1.70	0.97, 2.98
Province (Melanesians only)[a]						
South	69	31.4	70	41.4	1.00	Referent
North	60	27.3	47	27.8	1.33	0.83, 2.49
Loyalty Islands	91	41.4	52	30.8	1.91	1.15, 3.15
Years of education[b]						
Never went to school	22	7.5	20	5.7	1.10	0.55, 2.22
≤ 5 years	151	51.5	177	50.0	1.00	Referent
6–9 years	74	25.3	94	26.6	1.12	0.72, 1.76
≥ 10 years	22	7.5	44	12.4	1.22	0.62, 2.39
Missing	24	8.2	19	5.4	1.63	0.82, 3.21

CI confidence intervals; *OR* odds ratio

[a] OR adjusted for age

[b] OR adjusted for age and ethnicity

highest tertile among Melanesian women was 1.62 at the limit of statistical significance and the test for trend was 0.09. Again in European women, the odds ratio for cruciferous vegetables was below unity. Consumption of starchy food was slightly associated with thyroid cancer among Europeans only.

In Table 4, we defined two groups of women with low or high daily intake of iodine, using the median of the total daily iodine intake among controls as a cut-point (96 μg/day). The mean intake was estimated to be 62 and 143 μg iodine/day in the group below and above the median, respectively. Means in both groups were below the recommended daily iodine intake and correspond to moderate (30–74 μg/day) and mild iodine deficiency (75–149 μg/day) according to WHO criteria [19].

The consumption of cruciferous vegetables was associated with a significantly elevated odds ratio in women with low iodine intake (OR = 1.86, 95% CI: 1.01, 3.43; *p*-trend 0.06) but not in women with higher iodine intake (interaction $p = 0.33$). No modification effect was apparent for starchy food.

Discussion

We made the hypothesis that the very high incidence of thyroid cancer in New Caledonia was related to candidate risk factors such as iodine and goitrogens, and that the differences in thyroid cancer incidence across ethnic groups and geographic areas within the country could be explained by differences in dietary profiles. Although we included all incident cases that occurred in New Caledonia over a 6-year period, our study is based on a small population and had a limited statistical power, which precluded

Table 2 BMI, total energy intake, and mean daily intake of selected food items among control women by ethnic group and by Province of residence—New Caledonia, 1993–1999

Daily intake[b]	Melanesian			European	Other	p-value[a]
	South $n = 70$	North $n = 47$	Loyalty islands $n = 52$	$n = 110$	$n = 75$	
BMI (kg/m^2)	26.7	26.9	27.4	24.5	25.8	$p = 0.01$
Total energy intake (kcal)	1,995.1	2,397.3	2,036.4	1,954.7	2,207.8	$p = 0.04$
Salt water fish (g)	20.5	24.8	19.7	16.1	22.0	$p = 0.08$
Brackish water fish (g)	2.8	9.1	0.4	0.4	0.5	$p < 0.01$
Canned fish (g)	12.4	26.2	17.9	5.3	5.3	$p < 0.01$
Seafood (g)	12.3	9.9	5.5	9.6	6.5	$p = 0.29$
Milk (g)	120.1	44.8	50.3	150.1	152.9	$p = 0.01$
Dairy products (g)	57.2	23.7	29.7	127.3	89.8	$p < 0.01$
Dietary iodine (μg)	102.9	90.4	80.7	111.3	111.1	$p < 0.01$
Non cruciferous vegetables	152.7	150.3	209.5	209.9	170.1	$p = 0.01$
Cruciferous vegetables (g)[c]	53.8	62.2	83.3	56.5	51.7	$p = 0.02$
Cabbage	5.6	2.8	5.8	7.1	9.3	$p = 0.04$
Chinese cabbage	23.7	20.8	28.1	16.6	16.0	$p = 0.03$
Melanesian cabbage	10.1	20.5	32.7	1.2	0.9	$p < 0.01$
Starchy foods (g)[d]	75.2	240.7	136.5	40.4	72.8	$p < 0.01$
Cassava	20.0	54.0	16.0	2.7	6.9	$p < 0.01$

[a] Analysis of variance

[b] Mean values are adjusted for age (BMI and total energy intake) and adjusted for age and total energy intake for specific food items and iodine intake

[c] Cruciferous vegetables included cabbages, Chinese cabbage, Melanesian cabbage, cauliflower, broccoli, Brussels sprouts, turnips, and Swiss chard

[d] Starchy food included potatoes, cassava, sweet potatoes, yam, taro, and plantain

more detailed analyses by ethnic group and Province of residence. We did not find a consistent pattern of association between food items and thyroid cancer across population subgroups, but interesting clues emerged from the data.

An important strength of the study is the population-based design with exhaustive identification of thyroid cancer cases over the study period, and response rates close to 90% among eligible cases and controls. Unlike most previous studies on dietary factors in thyroid cancer, we used an extensive food frequency questionnaire with 110 foods items. We also used a food composition table of iodine content to estimate the daily intake of dietary iodine.

This method has several limitations. Recall bias may occur if study subjects report a different diet depending on their disease status, particularly if the cases are aware of a possible link between a risk factor and the disease. However, at the time of the study, no dietary recommendation program aiming at preventing thyroid diseases in New Caledonia had been conducted by the public health authorities, and the role of diet could not be suggested by the interviewers who were not aware of specific study hypotheses. It is thus very unlikely that the consumption of specific food items was reported differently by cases and controls.

It should also be pointed out that the cases of thyroid cancer were asked to report their dietary habits at the time of diagnosis, although they could be recruited up to 5 years after diagnosis. Reporting dietary habits with a lag of several years may be less accurate than reporting current diet. To avoid differential misclassification between cases and controls, we used a frequency-matched design where controls were attributed a year of reference similar to the year of diagnosis for the cases and were asked about their dietary habits using the same lag.

Another limitation of this study is the probable difference in iodine contents between food items consumed in metropolitan France, as reported in the food composition table, and food items actually consumed in New Caledonia. As some seafood from New Caledonia are not found in France, it is possible that our measure of daily iodine intake was slightly underestimated. In addition, the consumption of iodized salt could not be evaluated in our study. Alternative methods for measuring iodine intake include the 24-h measurement of urinary iodine, which is impractical in epidemiological studies. Neutron activation analysis has

Table 3 Odds ratios for thyroid cancer associated with selected food items among women, by ethnic group—New Caledonia, 1993–1999

	All ethnic groups					European					Melanesian				
	Quantity (g/day)	Ca (293)	Co (354)	OR[a]	95% CI	Quantity (g/day)	Ca (32)	Co (110)	OR[b]	95% CI	Quantity (g/day)	Ca (215)	Co (165)	OR[c]	95% CI
Salt water fish	<14.3	79	111	1.00	Referent	≤10.0	11	41	1.00	Referent	<22.5	53	53	1.00	Referent
	14.3–32.3	82	118	0.79	0.51, 1.22	10.0–25.9	5	31	0.57	0.17, 1.90	22.5–39.2	63	57	0.82	0.49, 1.36
	≥32.3	127	117	0.95	0.62, 1.46	>25.9	16	38	1.26	0.49, 3.23	≥39.2	79	55	1.07	0.64, 1.78
					p-trend = 0.15					*p-trend* = 0.78					*p-trend* = 0.12
Brackish water fish	0.0	254	304	1.00	Referent	0.0	30	105			0.0	185	129	1.00	Referent
	>0.0–10.0	27	30	0.81	0.46, 1.44	>0.0–2.3	1	4			>0.0–11.2	25	20	0.87	0.42, 1.79
	>10.0	12	20	0.43	0.20, 0.93	>2.3	1	1			>11.2	10	20	0.32	0.14, 0.77
					p-trend = 0.03										*p-trend* = 0.01
Seafood	≤1.5	90	116	1.00	Referent	≤2.6	9	44	1.00	Referent	≤1.3	69	57	1.00	Referent
	1.5–7.9	109	124	1.20	0.80, 1.79	2.6–7.9	12	31	1.95	0.70, 5.42	1.3–7.2	71	56	0.97	0.57, 1.63
	>7.9	94	114	1.02	0.67, 1.56	>7.9	11	35	1.24	0.43, 3.57	>7.2	80	56	1.23	0.72, 2.10
					p-trend = 0.37					*p-trend* = 0.86					*p-trend* = 0.47
Dairy products	≤40.6	121	116	1.00	Referent	≤98.1	9	37	1.00	Referent	≤17.6	84	55	1.00	Referent
	40.6–194.9	86	117	0.95	0.62, 1.45	98.1–405.0	14	36	1.35	0.48, 3.79	17.6–91.5	60	56	0.69	0.41, 1.16
	>194.9	86	121	1.03	0.67, 1.59	>405.0	9	37	0.73	0.23, 2.27	>91.5	76	58	1.00	0.59, 1.70
					p-trend = 0.85					*p-trend* = 0.32					*p-trend* = 0.19
Iodine intake (μg/day)	<75.0	106	117	1.00	Referent	<79.8	11	36	1.00	Referent	<68.1	70	55	1.00	Referent
	75.0–112.6	83	117	1.15	0.73, 1.80	79.8–114.0	5	36	0.26	0.06, 1.07	68.1–107.1	70	56	1.13	0.63, 2.00
	≥112.6	104	120	1.13	0.68, 1.87	≥114.0	16	38	0.53	0.14, 1.97	≥107.1	80	58	1.38	0.71, 2.68
					p-trend = 0.43					*p-trend* = 0.95					*p-trend* = 0.30
Cruciferous vegetables	≤27.8	74	116	1.00	Referent	≤25.7	15	37	1.00	Referent	≤28.6	54	56	1.00	Referent
	27.8–65.4	98	118	1.11	0.73, 1.69	25.7–66.8	7	36	0.49	0.16, 1.47	28.6–66.4	72	56	1.23	0.72, 2.10
	>65.4	121	120	1.39	0.91, 2.11	>66.8	10	37	0.46	0.16, 1.37	>66.4	94	57	1.62	0.94, 2.80
					p-trend = 0.11					*p-trend* = 0.22					*p-trend* = 0.09
Starchy food	≤8.8	51	114	1.00	Referent	0.0	13	56	1.00	Referent	≤50.4	73	56	1.00	Referent
	8.8–74.7	109	118	1.22	0.76, 1.97	>0.0–14.8	4	27	0.68	0.19, 2.37	50.4–133.3	77	58	0.92	0.54, 1.57
	>74.7	133	121	1.05	0.62, 1.78	>14.8	15	27	2.27	0.84, 6.13	>133.3	70	54	0.84	0.44, 1.61
					p-trend = 0.74					*p-trend* = 0.05					*p-trend* = 0.60

Table 3 continued

	All ethnic groups					European					Melanesian				
	Quantity (g/day)	Ca (293)	Co (354)	OR[a]	95% CI	Quantity (g/day)	Ca (32)	Co (110)	OR[b]	95% CI	Quantity (g/day)	Ca (215)	Co (165)	OR[c]	95% CI
Cassava	0.0	98	177	1.00	Referent	0.0	20	88	1.00	Referent	≤6.6	64	51	1.00	Referent
	0.0–14.3	86	86	1.23	0.81, 1.89	>0.0–6.6	6	15	1.97	0.61, 6.34	6.6–28.6	69	48	0.86	0.52, 1.42
	>14.3	107	89	1.24	0.80, 1.91	>6.6	6	7	2.52	0.65, 9.75	>28.6	85	68	1.18	0.67, 2.07
					p-trend = 0.50					*p-trend* = 0.12					*p-trend* = 0.55

Ca cases; *CI* confidence intervals; *Co* controls; *OR* odds ratio

[a] Adjusted for age, total energy intake, ethnicity

[b] Adjusted for age, total energy intake

[c] Adjusted for age, total energy intake, and Province of residence

also been used in one study to measure iodine content in toenail clippings [20], but this technique provides an integrated measure of iodine exposure over a 2–4-week period approximately 1 year prior to clipping. The iodine exposure estimate based on the food frequency questionnaire used in our study constituted an alternative to laboratory measurements. Although imprecise and entailing nondifferential exposure misclassification, it was deemed adequate for estimating the average daily iodine intake over the past few years. The estimate of mean daily intake in our study subjects was 100 μg iodine, a value corresponding to mild iodine deficiency. This result is consistent with a survey carried out in a sample of tribes and communes in New Caledonia based on iodine measurements in urinary samples (unpublished data: http://www.wpro.who.int/NR/rdonlyres/FAF55745-689B-4CAE-87B6-BDCE7950BC3F/0/nec.pdf).

Fish and seafood

We found that the consumption of saltwater fish, canned fish, and seafood was not related to thyroid cancer risk. Brackish water fish, almost exclusively consumed by Melanesians from mainland New Caledonia (Northern and Southern Provinces) was inversely related to the disease. A pooled analysis of 13 case–control studies, conducted in Europe, USA, and Asia, reported no overall association of thyroid cancer with fish and shellfish consumption, but results were conflicting across populations [21]. Additional studies alternatively reported positive associations with fish sauce, dried or salted fish [11] or processed fish products [22], and negative associations with saltwater fish [23] or fresh fish [22]. These inconsistencies between studies may be explained by differences in local iodine availability, and the assumption that high consumption of fish or seafood is protective in areas with severe iodine deficiency, deleterious in areas where iodine is readily available, and has no effect in areas where iodine intake is adequate. This hypothesis is supported in the pooled analysis [21] by the observation of a slight negative association of fish intake with thyroid cancer in areas where iodine deficiency is or was common. The absence of an association between fish and seafood consumption and thyroid cancer in New Caledonia also fits this hypothesis, as only mild iodine deficiency is observed in this country.

Dairy products

The presence of iodine in milk and dairy products is mainly due to the iodophor sanitizing solutions used in the dairy industry. In New Caledonia, no association with dairy products was detected. One study conducted in Norway and Sweden [24] reported an increased risk of

Table 4 Odds ratios for thyroid cancer associated with cruciferous vegetables and starchy food by iodine intake (below or above median) among women—New Caledonia, 1993–1999

	Iodine intake								Interaction test
	<96.0 μg/day				≥96.0 μg/day				
	Ca (149)	Co (175)	OR	95% CI	Ca (144)	Co (179)	OR	95% CI	
Cruciferous vegetables									
≤27.8	38	67	1.00	Referent	36	49	1.00	Referent	
27.8–65.4	58	63	1.47	0.82, 2.61	40	55	0.77	0.41, 1.46	
>65.4	53	45	1.86	1.01, 3.43	68	75	0.98	0.55, 1.77	
				p-trend = 0.06				*p-trend* = 0.76	*p* = 0.33
Starchy foods									
≤8.8	25	57	1.00	Referent	26	57	1.00	Referent	
8.8–74.7	70	65	1.49	0.77, 2.89	39	53	1.01	0.50, 2.05	
>74.7	54	52	1.07	0.50, 2.3	79	69	1.07	0.51, 2.26	
				p-trend = 0.76				*p-trend* = 0.26	*p* = 0.86

OR are adjusted for age, total energy intake, and ethnic group

Ca cases; *CI* confidence intervals; *Co* controls; *OR* odds ratio

thyroid cancer in endemic goiter areas related to high intake of dairy products. It should be noted that the consumption of dairy products was low in New Caledonia as the highest tertile was >195 g/day in comparison with the Nordic study where the lowest tertile was <180 g/day.

Daily iodine intake

Our data do not provide strong evidence that dietary iodine intake is related to thyroid cancer, although it was negatively but not statistically significantly associated with the disease in European women. In other case–control studies that assessed daily iodine intake from the diet, the Hawaii study [10] reported an elevation in risk (OR = 1.6; 95% CI: 0.8–3.2) and the San Francisco Bay area study [11] reported an inverse association (OR = 0.49; 95% CI: 0.29, 0.84) in the highest exposure categories. In the later study, no association with biomarkers of iodine exposure from nail clipping was observed. Both studies were conducted in a multiethnic population with wide variations of iodine intake. Very high levels of iodine intake, i.e., two to three times the recommended daily allowance of 150 μg/day [19], were measured in these studies when compared to the mean intake of 100 μg/day in New Caledonia. The inconsistencies between studies suggest that interactions between dietary and other population-specific risk factors related to lifestyle or environment may exist.

Goitrogenic food groups

There was some indication of a positive association between consumption of cruciferous vegetables and thyroid cancer in Melanesian women. This association was negative, but not statistically significant, in European women. The mean consumption of cruciferous vegetables in Melanesian women was about 70 g/day, a relatively high value in comparison with the average cruciferous vegetable intake of 25–30 g/day in North America, 15–30 g/day in Europe and 40–80 g/day in Asia [25]. The consumption of cruciferous vegetables was thus a possible candidate for explaining the elevated incidence of thyroid cancer in this ethnic group. The stronger association of cruciferous vegetables with thyroid cancer (OR = 1.86, 95% CI: 1.01, 3.43) in women with daily iodine intake below 96 μg/day, i.e., with moderate iodine deficiency, is of particular interest. This finding is consistent with biological mechanisms indicating that goitrogenic substances contained in cruciferous vegetables inhibit iodine absorption by the thyroid, thus increasing iodine deficiency within the thyroid gland, and thyroid cell growth through TSH stimulation [13]. In the pooled analysis of 11 case–controls studies [14], cruciferous vegetables were not associated with thyroid cancer, and no difference between iodine-rich or iodine-deficient areas was apparent. However, among Japanese subjects with more frequent consumption of cruciferous vegetables, an elevated odds ratio was reported [14]. High consumption of cruciferous vegetables was associated with increased risk in persons who ever lived in areas of endemic goiters in Sweden [24]. An additional study conducted in Kuwait [22] reported an increased risk of thyroid cancer in frequent consumers of cabbage or cauliflower. Conversely, US studies from Los Angeles and Hawaii reported a decreasing risk with frequent intake of turnips and rutabagas (p-trend = 0.01) [23] and a negative association with high consumption of cruciferous vegetables [10]. As noted previously, these studies were conducted in populations where very high iodine intakes were observed. To our knowledge, no study has previously investigated the role of cruciferous vegetables in persons with low iodine intake assessed at an individual level, as we did in New Caledonia. This result has strong possible biological grounds and should be confirmed in larger studies.

Thyroid cancer was weakly associated with starchy food in Europeans. Because Europeans had very low consumption of starchy food, this association could be due to chance or possibly to another food item associated with starchy food consumption in this subgroup. We also studied the role of cassava, known to have goitrogenic properties [26, 27], but no association with thyroid cancer emerged. To our knowledge, no previous epidemiological study has examined the role of cassava consumption in thyroid cancer.

Our results did not support the hypothesis that the consumption of fish and seafood is related to thyroid cancer, but suggest a positive association between the consumption of cruciferous vegetables and thyroid cancer. In addition, the possible interaction between consumption of cruciferous vegetables and low intake of dietary iodine may constitute an important finding in our study that should be further scrutinized. Since the consumption of cruciferous vegetables is higher and the iodine deficiency is possibly stronger in Melanesian women than in other ethnic groups, these dietary factors may contribute, along with other anthropometric or reproductive risk factors previously identified in this study, to explain the exceptionally high incidence of thyroid cancer in this group.

Acknowledgments The authors wish to thank Dr. Jean-Paul Grangeon (Direction des Affaires Sanitaires et Sociales Nouvelle-Calédonie) as well as the Provincial Health Authorities (DPASS Sud, DPASS Nord, DPASS Îles) for their support during data collection. They are particularly grateful to Michèle Reynier who coordinated the interviews of study subjects across New Caledonia. They also thank Dr. Pierre Valeix for the iodine content data and Alexandra Suprayen for her help in quantifying local food portion size.

Conflict of interest statement This study was supported by grants from the "Fondation de France," the "Association pour la Recherche contre le Cancer," and the "Agence Française de Sécurité Sanitaire de l'Environnement et du Travail (AFSSET)".

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