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Cell phone use and risk of thyroid cancer: a population-based case-control study in Connecticut

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Abstract

Purpose: This study aims to investigate the association between cell phone use and thyroid cancer.

Methods: A population-based case-control study was conducted in Connecticut between 2010 and 2011 including 462 histologically confirmed thyroid cancer cases and 498 population-based controls. Multivariate unconditional logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (95% CI) for associations between cell phone use and thyroid cancer.

Results: Cell phone use was not associated with thyroid cancer (OR: 1.05, 95% CI: 0.74–1.48). A suggestive increase in risk of thyroid microcarcinoma (tumor size ≤10mm) was observed for long-term and more frequent users. Compared to cell phone non-users, several groups had nonstatistically significantly increased risk of thyroid microcarcinoma: individuals who had used a cell phone >15 years (OR: 1.29, 95% CI: 0.83–2.00), who had used a cell phone >2 hours per day

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

(OR: 1.40, 95% CI: 0.83–2.35), who had the most cumulative use hours (OR: 1.58, 95% CI: 0.98–2.54), and who had the most cumulative calls (OR: 1.20, 95% CI: 0.78–1.84).

Conclusion: This study found no significant association between cell phone use and thyroid cancer. A suggestive elevated risk of thyroid microcarcinoma associated with long-term and more frequent uses warrants further investigation.

Keywords

Thyroid cancer; Cell phone; Case-control study; Non-ionizing radiation

INTRODUCTION

Thyroid cancer remains the fastest increasing cancer in the United States and its incidence rate has nearly tripled since the 1980s from 4.3/100,000 in 1980 to 15.0/100,000 in 2014 [1]. It is now the fifth most common cancer among women in the United States [1]. While the incidence rate has continually increased, the mortality rate has remained relatively stable at 0.5/100,000 in both 1980 and 2013 [1, 2]. Though investigators offered various explanations for the increasing incidence of thyroid cancer, consensus has not been reached. Over-diagnosis is estimated to account for 50% of the variability of thyroid cancer incidence in the United States [3–5], suggesting that other factors, such as changing environmental and/or lifestyle factors have also contributed to the increase [6–9].

The thyroid gland is sensitive to radiation. Ionizing radiation has been classified as a known human carcinogen (Group 1) by the International Agency for Research on Cancer (IARC) due to its ability to transfer high energy to biological molecules and directly damage DNA [10]. It is also the only established environmental risk factor for thyroid cancer [11]. A recent analysis by our research group reported that increased exposure to diagnostic radiography was associated with the risk of thyroid cancer, especially for thyroid microcarcinomas [12]. A different study observed that nearly 40% of the increase in thyroid cancer could be attributed to exposure to computerized tomography (CT) scanning before age 19 [13].

The effects of non-ionizing radiation (NIR), however, remain under-investigated. Cell phones, which emit radiofrequency energy, a form of NIR, are currently used by millions of people worldwide, raising concerns about potential harmful effects of this widespread exposure. IARC classified radiofrequency electromagnetic fields from use of personal devices including cell phones as a Group 2B possible human carcinogen based on limited evidence on humans [14]. This low-frequency electromagnetic radiation has enough energy to heat and vibrate molecules, but lacks sufficient energy to remove electrons from atoms and molecules and break molecular bonds. Evidence from in vitro studies also suggests that NIR can lead to higher levels of reactive oxygen species in human blood cells, neuronal cells and spermatozoa, increasing oxidative stress and resulting in DNA damage [15]. Most epidemiologic studies of potential health effects of cell phone use have focused on brain tumors at the outcome. While results have been primarily null [16–21], some studies have suggested the possibility of an effect at the highest exposure categories [22–27]. Based on these population studies, the IARC Working Group concluded that these observed

statistically significant associations, though vulnerable to methodological limitations and possible biases, could not be d ismissed [28]. To date, no study has comprehensively investigated the association between cell phone use and risk of thyroid cancer, even though the thyroid gland is the most radiosensitive organ in the body. Furthermore, the thyroid gland's location in the neck places it in close proximity to NIR emissions from cell phones when held to the ear. The estimated average specific absorption rate (SAR) of the thyroid gland for near-field exposure from a cell phone at 1800 MHz is higher than the SARs of most organs and tissues except those associated with the brain [29]. Considering the increasing incidence of thyroid cancer and uncertain effects of cell phone use on thyroid cancer, we analyzed data from a population-based case-control study in Connecticut to examine the association between thyroid cancer and cell phone use.

METHODS

This population-based case-control study has been described previously [12]. In brief, the study included 462 histologically confirmed incident thyroid cancers (papillary (ICD-O-3: 8050, 8052, 8130, 8260, 8340–8344, 8450, and 8452), follicular (ICD-O-3: 8290, 8330–8332, and 8335), medullary (ICD-O-3: 8345, 8346, and 8510), or anaplastic (ICD-O-3: 8021)) diagnosed between 2010 and 2011 in Connecticut, and 498 population-based controls. All cases were between 21 and 84 years old, without previous cancer except nonmelanoma skin cancer, and were alive at the time of interview. A total of 701 eligible cases were identified and 462 (65.9%) completed in-person interviews. Controls were recruited through random digit dialing. A total of 498 controls joined the study with a participation rate of 61.5%. All participants, including cases and controls in this study, were interviewed by trained study interviewers using a standardized and structured questionnaire to collect information on demographics, cell phone use, radiation exposure, lifestyle factors, occupation, and diet. Cases and controls were frequency-matched by age (±5 years). The study was approved by the Human Investigations Committee at Yale and the Connecticut Department of Public Health. Written informed consent was obtained from all participants.

The participants were asked the following questions regarding the frequency, duration, and protective behaviors of cell phone use: (1) Have you ever used a cell phone at least once a week for 6 months prior to one year before diagnosis? (2) What calendar year did you start regularly using a cell phone? (3) What calendar year did you stop regularly using cell phone? (4) Excluding the time period that you did not use a cell phone, altogether how many years have you regularly used a cell phone? (5) What proportion of the time did you use a hands-free device when you regularly used a cell phone? (6) On average, how many phone calls did you make or receive per day? (7) On average, how many hours per day did you use cell phone? If a participant answered "Yes" to question (1), he/she was defined as a "cell phone user" and otherwise a "cell phone non-user". Information on cordless phone use was not collected in our study. Cumulative cell phone use was estimated by multiplying cell phone use hours or calls per day with the duration of use. Each variable was categorized into tertiles based on its distribution among controls.

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using unconditional logistic regression models. The associations were estimated for overall population and by

histologic subtype and tumor size. All controls were used in stratified analyses. Associations of cumulative use were further estimated by the duration of cell phone use. All ORs were adjusted for age (continuous), sex (male, female), education (<college, college, >college), family history of thyroid cancer (yes, no), alcohol consumption (yes, no), body mass index (BMI, <25, 25–29.9, ≥30 kg/m2), previous benign thyroid diseases (yes, no), occupational radiation exposure (yes, no), and radiation treatment (yes, no). Additional adjustment for variables, including race, smoking, family income, diagnostic radiation exposure, dietary intake of seafood and iodine intake did not substantially change (10%) the observed associations; therefore, these variables were not included in the final models. For the subgroup analysis among women, additional adjustment for age at menarche, menopausal status, and parity did not change the observed association. All tests of statistical significance were two-sided. All analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, North Carolina, USA).

RESULTS

Of the 462 cases, there were 392 (84.8%) diagnosed with papillary thyroid cancer, 56 (12.1%) follicular, 12 (2.6%) medullary, 1 (0.2%) anaplastic, and 1 (0.2%) other thyroid cancer. A total of 217 cases were microcarcinomas (≤10 mm). Mean age at diagnosis of the case group was 51.2, three years younger than that of control group. Cases were more likely to be female, be exposed to occupational radiation, be less educated, have a higher BMI, and have a family history of thyroid cancer and a previous diagnosis of benign thyroid disease (Table 1). Differences in family income, race, and smoking between cases and controls were not statistically significant.

The proportion of cell phone users was 77.9% among cases and 75.5% among controls (P=0.376). The mean age was 50.7 years for cell phone users and 59.2 years for non-users. The distributions of the cell phone use metrics were similar among cases and controls. The mean age at first use was 35.9 years (range: 11 to 72 years) for cases and 38.9 years (range: 9 to 71 years) for controls. Cases and controls each had a median of 5 calls per day, though the range was a little greater for cases (<1 to 100 calls per day) compared to controls (1 to 60 calls per day). Years of use were also similar, ranging from 1 to 35 years with a median of 13 for cases and from 2 to 33 years with a median of 13 for controls. Median duration of daily usage was 1 hour for both cases and controls with a range of <1 to 10 hours per day for cases and <1 to 15 hours per day for controls. Only 19 participants reported using hands-free devices in total, 9 were cases and 10 were controls.

Using a cell phone was not significantly associated with an increased risk of thyroid cancer (OR: 1.05, 95% CI: 0.74–1.48, Table 2). No statistically significant association was observed in relation to number of daily calls. However, compared to non-users, greater daily hours of use and longer duration of use showed a suggestive increase in thyroid cancer risk (1–2 hours per day: OR: 1.51, 95% CI: 0.90–2.53; >2 hours per day: OR: 1.40, 95% CI: 0.83–2.35; >15 years: OR: 1.29, 95% CI: 0.83–2.00). There was no significant association with using hands-free device or the age at first use of a cell phone. When stratified by gender, a suggestive association was observed for male using cell phone >15 years (OR:

2.11, 95% CI: 0.91–4.89), and female using cell phone > 2 hours per day (OR: 1.52, 95% CI: 0.83–2.80).

For cumulative use of cell phone, users in the highest tertile of total use hours experienced a borderline significantly increased risk of thyroid cancer compared to non-users (OR: 1.58, 95% CI: 0.98–2.54). In stratified analyses, this trend was also observed for females (OR: 1.63, 95% CI: 0.93–2.86), but not males (Table 2).

We further conducted analyses stratified by histologic subtype (Table 3) and by tumor size (Table 4, only for well-differentiated cases). Well-differentiated (papillary and follicular) and papillary only thyroid cancers showed similar patterns, no significant association was observed. Follicular and other subtypes of thyroid cancers were not analyzed separately because of limited sample sizes. A suggestive increased risk associated with long-term and frequent uses were observed for thyroid microcarcinomas, but not larger tumors (>10mm).

Table 5 showed the results of combined analysis of latency and cumulative use. In latency group, compared to cell phone non-users, no statistically significant association between cumulative cell phone use and thyroid cancer was observed.

DISCUSSION

In this population-based case-control study in Connecticut, cell phone use was not significantly associated with an increased risk of thyroid cancer. While there were suggestive elevated risks for long-term and frequent cell phone use, particularly among females and for microcarcinoma, no monotonic gradient was observed across any of these findings.

As a Group 2B possible human carcinogen, health effects of NIR from cell phone has been a concern for many years. Though heating is the only established biological effect from NIR, evidence suggests additional possible mechanisms. Animal studies found that NIR caused oxidative stress [31], changes in protein structure and function [32], and increased oxidative DNA damage [15, 33, 34]. It was also suggested that energy from NIR could alter the structure and function of proteins involved in DNA repair mechanisms [33]. Increased DNA damage has been consistently associated with increased risk of multiple cancers, including thyroid cancer [35]. One study reported a statistically significant association between cell phone use and alterations in thyroid stimulating hormone (TSH) [36]. Alterations in TSH levels have been linked to an increased risk of thyroid cancer, though the results from epidemiologic studies have been inconsistent [37–40]. While the mechanisms linking TSH levels to thyroid cancer have not been fully understood, higher TSH may promote cancer growth [41]. Additionally, TSH can stimulate the generation of hydrogen peroxide (H_2O_2) in the thyroid gland [42]. H_2O_2, a major source of free radical, can increase oxidative DNA damage in thyroid tissue and induce cancer initiation [42].

The world-wide increase of thyroid cancer incidence, has paralleled with an increase in cell phone use over the past decades [43–45]. While there is a speculation that increased cell phone use might increase the risk of thyroid cancer [43], very few epidemiologic studies have confirmed the association. One prospective cohort study of 791,710 UK women conducted by Benson et al. looked at the association between cell phone use and risk of

various cancers including thyroid cancer [18]. A total of 345 incident thyroid cancer cases were identified during the study follow-up period. The study found no statistically significant association between cell phone use and risk of thyroid cancer (RR: 1.07, 95% CI: 0.85, 1.35 for ever used cell phone and RR: 1.06, 95% CI: 0.71, 1.61 for user >10 years), which was consistent with our study. While the prospective study design avoided potential differential recall bias, the study lacked information on daily frequency use of cell phone and tumor subtypes.

Compared to Benson's study [18], our study reported the longest duration of cell phone use. 129 and 99 thyroid cancer cases in our study reported using cell phone 12–15 years and >15 years, respectively, only 32 thyroid cancer cases in Benson's study reported using cell phone for more than 10 years. A suggestive increased risk was only observed among those who had used cell phone for more than 15 years in our study. Future studies should explore with more attention at the long-term exposure group. We also observed that suggestive findings related to long term and more frequent cell phone use showed slightly gender difference. Because the difference was not statistically significant and the sample size of male participants was small, chance findings cannot be ruled out. Future larger study with sufficient power is needed to examine the association by gender.

In addition, an elevated risk associated with long-term or more frequent use of cell phone was only observed for microcarcinoma but not larger tumors in our study. While the chance findings cannot be ruled out, several potential explanations are worth considering. It was possible that long-term and frequent cell phone users had better health access due to their higher socioeconomic status (SES) (significant positive correlations between SES and years of cell phone use: correlation coefficient=0.22 ($P < 0.01$) for family income and 0.13 ($P < 0.01$) for education), thus, their thyroid tumors were more likely to be diagnosed earlier. It has been reported that incidence of thyroid cancer, particularly small tumors, increases with increasing socioeconomic status [46]. We performed stratified analysis by education level and family income and found no differences in the observed associations. It was also possible that cellphone-associated thyroid carcinoma constitutes a new disease entity.

When interpreting the study findings, potential limitations must be considered. Information on cell phone use was based on self-report, therefore, participants may have difficulty accurately recalling use and potential differential over-reporting of cell phone use might occur if patients believe that cell phone use increases their thyroid cancer risk. However, early studies provided no evidence on differential over-reporting of cell phone use between cancer cases and noncancer controls [23, 24, 47, 48]. In addition, there was no existing literature linking cell phone use and thyroid cancer during the study period that could have influenced participant's risk perceptions. Moreover, the lack of association between cell phone use of thyroid cancer, as well as a suggestive increase in risk among long term and frequent cell phone users mainly observed for microcarcinomas argues against recall bias playing a major role in the observed associations. Therefore, if there was recall bias, it was likely to be non-differential and resulted in an underestimation of the true association. Another possible explanation for our null findings was that the majority of study participants did not start using cell phones until age 21; therefore, the exposure may have occurred after the etiologically relevant time window for thyroid cancer.

Exposure misclassification is another concern. Using a hands-free device might have different exposure level. However, few people in this study used a hands-free device, which hampered examination of the association. Information on cordless phone use was not collected. These users were likely to be classified as unexposed group, which could potentially bias the results toward null. NIR emitted from cell phone varies among different cell phones [43] which could cause exposure misclassification. However, this misclassification was likely non-differential. Future studies could use carrier records in conjunction with self-reported use to improve accuracy of exposure assessment. However, some studies have demonstrated moderate correlation between objective records and self-reported use [49], and carrier records do not provide information about use of hands-free devices or the speaker function, which also influences radiation exposure. While a number of confounding variables have been controlled in our models, potential residual confounding effect cannot be ruled out.

Our study was conducted in 2010–2011, when smartphones were getting introduced to the market. The transition to smartphone has seen a major change in how cell phones are used (e.g., texting versus phone calls). Because of the continually changing cell phone technology and the changing relationships people have with their cell phones, this study results might not be generalizable to current smart phone users.

Finally, our study participation rates (65.9% and 61.5% for cases and controls, respectively) were relatively low compared to some previous studies [19, 20, 22, 26] but were comparable to those in INTERPHONE and CERENAT studies [23, 24]. We compared the distributions of age, gender, and race between participants and non-participants for both cases and controls and found no statistically significant differences. The rates of cell phone users in our study were 75.5% in controls and 77.9% in cases, which were comparable to the estimated cell phone users (80%) in the US adults in 2010 [50].

In conclusion, this study found no statistically significant association between cell phone use and thyroid cancer. Potential increased risk of thyroid cancer among long-term and frequent cell phone users found in our study warrant further investigation.

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ABBREVIATIONS

CI	Confident interval
IARC	International Agency for Research on Cancer
NIR	Non-ionizing radiation
OR	Odds ratio
SES	Socioeconomic status
TSH	Thyroid stimulating hormone

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Table 1.

Distribution of selected characteristics of the study population

	Case (n=462) n (%)	Controls (n=498) n (%)	P-value
Age (years)			
Mean (SD)	51.2 (12.3)	54.2 (13.2)	<0.01
<40	86 (18.6)	64 (12.8)	
40–49	115 (24.9)	123 (24.7)	
50–59	149 (32.3)	139 (27.9)	
60–69	81 (17.5)	100 (20.1)	
≥70	31 (6.7)	72 (14.5)	<0.01
Sex			
Female	375 (81.2)	344 (69.1)	
Male	87 (18.8)	154 (30.9)	<0.01
Race			
White	415 (89.8)	450 (90.5)	
Black	18 (3.9)	25 (5.0)	
Other	29 (6.3)	23 (4.5)	0.13
Years of education			
High school or lower	160 (34.6)	113 (22.7)	
College	185 (40.0)	236 (47.4)	
Graduate school	113 (24.5)	143 (28.7)	
Missing	4 (0.9)	6 (1.2)	<0.01
Family income *per capita*			
Low	128 (27.7)	133 (26.7)	
Medium	113 (24.5)	131 (26.3)	
High	74 (16.0)	82 (16.5)	
Confidential or unknown	147 (31.8)	152 (30.5)	0.90
Family history of thyroid cancer among first-degree relatives			
Yes	72 (15.6)	48 (9.6)	
No	390 (84.4)	450 (90.4)	0.03
Prior benign thyroid disease[a]			
Yes	62 (13.4)	14 (2.8)	
No	400 (86.6)	484 (97.2)	<0.01
Radiation treatment[b]			
Yes	14 (3.0)	48 (9.6)	
No	448 (97.0)	496 (99.6)	<0.01
Occupational radiation exposure			
Yes	41 (8.9)	31 (6.2)	
No	403 (87.2)	460 (92.4)	
Missing or unknown	18 (3.9)	7 (1.4)	0.01
Diagnostic radiation exposure prior to diagnosis			

	Case (n=462) n (%)	Controls (n=498) n (%)	P-value
Yes	424 (91.8)	442 (88.8)	
No	38 (8.2)	56 (11.2)	0.12
Body mass index (kg/m^2)			
<25	145 (31.4)	203 (40.8)	
25 to <30	146 (31.6)	168 (33.7)	
30+	166 (35.9)	118 (23.7)	
Missing	5 (1.1)	9 (1.8)	<0.01
Smoking[c]			
Yes	141 (30.5)	172 (34.5)	
No	321 (69.5)	321 (65.5)	0.18
Alcohol consumption[d]			
Yes	188 (40.7)	267 (53.6)	
No	274 (59.3)	231 (46.4)	<0.01

SD: standard deviation

[a] Benign thyroid disease included hyperthyroidism, hypothyroidism, goiter, thyroid nodules, and thyroid adenoma.

[b] Radiation treatment: a history of therapeutic external beam radiation treatment.

[c] Ever smoking was defined as ever smoked a total of 100 cigarettes or more.

[d] Ever alcohol consumption was defined as ever had more than 12 drinks of alcoholic beverages such as beer, wine, or liquor. 1 drink of beer = 1 can or bottle; 1 drink of wine = 14 oz glass; 1 drink of liquor = 1 shot.

Table 2.

Associations between cell phone use and risk of thyroid cancer

		Overall			Male			Female		
Cell phone user	**Control**	**Case**	**OR (95% CI)[a]**	**P for trend**	**Case**	**OR (95% CI)[a]**	**P for trend**	**Case**	**OR (95% CI)[a]**	**P for trend**
No	122	102	1.00		18	1.00		84	1.00	
Yes	376	360	1.05 (0.74, 1.48)		69	1.27 (0.62, 2.61)		291	0.99 (0.66, 1.47)	
Hands-free device										
Yes	10	9	1.15 (0.43, 3.08)		1	1.27 (0.62, 2.62)		8	0.98 (0.65, 1.47)	
No	366	351	1.05 (0.74, 1.48)		68	1.18 (0.06, 22.46)		283	1.16 (0.40, 3.37)	
Daily use hour				0.102			0.913			0.082
≤1 hours/day	137	124	1.10 (0.72, 1.66)		25	1.76 (0.72, 4.32)		99	0.97 (0.60, 1.56)	
1–2 hours/day	47	60	1.51 (0.90, 2.53)		13	1.66 (0.57, 4.82)		47	1.45 (0.79, 2.65)	
>2 hours/day	52	61	1.40 (0.83, 2.35)		12	1.05 (0.35, 3.14)		49	1.52 (0.83, 2.80)	
Daily phone call				0.392			0.307			0.728
≤3 calls/day	141	122	0.95 (0.63, 1.42)		14	0.68 (0.27, 1.73)		108	1.01 (0.64, 1.59)	
3–6 calls/day	112	99	0.98 (0.63, 1.50)		23	1.57 (0.65, 3.78)		76	0.84 (0.51, 1.38)	
>6 calls/day	105	113	1.19 (0.77, 1.84)		26	1.22 (0.51, 2.92)		87	1.17 (0.70, 1.94)	
Phone use year				0.337			0.101			0.910
≤12 years	138	128	0.99 (0.66, 1.49)		17	0.99 (0.39, 2.48)		111	0.97 (0.61, 1.53)	
12–15 years	143	129	0.94 (0.63, 1.42)		19	0.82 (0.34, 1.97)		110	0.97 (0.61, 1.55)	
>15 years	92	99	1.29 (0.83, 2.00)		31	2.11 (0.91, 4.89)		68	1.03 (0.62, 1.73)	
Age at first use				0.828			0.680			0.992
≤20 years old	34	47	1.08 (0.53, 2.20)		9	1.49 (0.34, 6.01)		38	0.95 (0.42, 2.18)	
21–50 years old	267	260	1.06 (0.72, 1.55)		48	1.44 (0.65, 3.17)		212	0.96 (0.62, 1.49)	
>50 years old	75	53	1.03 (0.62, 1.70)		12	0.99 (0.36, 2.70)		41	1.05 (0.58, 1.90)	
Cumulative use hour				0.072			0.493			0.094
≤4,745 hours	92	85	1.10 (0.70, 1.74)		14	1.91 (0.68, 5.38)		71	0.98 (0.58, 1.63)	
4,745–9,490 hours	75	72	1.13 (0.71, 1.82)		14	1.31 (0.46, 3.72)		58	1.08 (0.63, 1.85)	
>9,490 hours	68	87	1.58 (0.98, 2.54)		21	1.55 (0.61, 3.96)		66	1.63 (0.93, 2.86)	
Cumulative phone call				0.535			0.141			0.843
≤14,235 calls	131	119	1.01 (0.67, 1.52)		11	0.69 (0.25, 1.86)		108	1.06 (0.67, 1.67)	

		Overall			Male			Female		
Cell phone user	Control	Case	OR (95% CI)[a]	P for trend	Case	OR (95% CI)[a]	P for trend	Case	OR (95% CI)[a]	P for trend
14,235–32,850 calls	116	98	0.87 (0.56, 1.35)		16	0.86 (0.34, 2.19)		82	0.86 (0.52, 1.42)	
>32,850 calls	108	114	1.20 (0.78, 1.84)		34	1.65 (0.71, 3.81)		80	1.02 (0.61, 1.70)	

CI, confidence interval; OR, odds ratio

[a]Adjusted for age (continuous), sex (male, female), education (<college, college, >college), family history of thyroid cancer (yes, no), alcohol consumption (yes, no), BMI (<25, 25–29.9, ≥30 kg/m2), previous benign thyroid disease (yes, no), occupational radiation exposure (yes, no), and radiation treatment (yes, no).

Table 3.

Associations between cell phone use and risk of thyroid cancer by histologic subtype

	Well-differentiated			Papillary		
Cell phone user	**Case**	**OR (95% CI)[a]**	**P for trend**	**Case**	**OR (95% CI)[a]**	**P for trend**
No	94			82		
Yes	350	1.04 (0.73, 1.48)		306	1.02 (0.71, 1.47)	
Hands-free device						
Yes	9	1.19 (0.44, 3.23)		8	1.24 (0.45, 3.46)	
No	341	1.04 (0.73, 1.48)		298	1.01 (0.70, 1.46)	
Daily use hour			0.122			0.177
≤1 hours/day	121	1.10 (0.72, 1.67)		106	1.07 (0.69, 1.66)	
1–2 hours/day	57	1.45 (0.86, 2.45)		49	1.33 (0.77, 2.30)	
>2 hours/day	59	1.39 (0.82, 2.35)		52	1.38 (0.80, 2.38)	
Daily phone call			0.453			0.610
≤3 calls/day	119	0.95 (0.63, 1.42)		104	0.95 (0.62, 1.44)	
3–6 calls/day	97	0.97 (0.62, 1.50)		83	0.93 (0.59, 1.46)	
>6 calls/day	109	1.17 (0.75, 1.81)		97	1.12 (0.71, 1.78)	
Phone use year			0.434			0.467
≤12 years	126	1.00 (0.67, 1.51)		105	0.95 (0.62, 1.46)	
12–15 years	127	0.95 (0.63, 1.43)		117	0.95 (0.62, 1.45)	
>15 years	93	1.24 (0.80, 1.94)		80	1.21 (0.76, 1.91)	
Age at first use			0.824			0.896
≤20 years old	46	1.01 (0.49, 2.08)		44	1.12 (0.54, 2.33)	
21–50 years old	254	1.05 (0.72, 1.55)		225	1.08 (0.72, 1.60)	
>50 years old	50	1.02 (0.61, 1.71)		37	0.87 (0.50, 1.51)	
Cumulative use hour			0.096			0.169
≤4,380 hours	84	1.12 (0.71, 1.77)		74	1.11 (0.69, 1.79)	
4,380–13140 hours	68	1.08 (0.67, 1.75)		59	1.02 (0.61, 1.68)	
>13,140 hours	84	1.56 (0.96, 2.51)		73	1.50 (0.91, 2.47)	
Cumulative phone call			0.664			0.830
≤10,220 calls	117	1.02 (0.67, 1.54)		101	1.02 (0.66, 1.56)	
10,220–41,975 calls	96	0.86 (0.56, 1.34)		83	0.82 (0.52, 1.29)	
>41,975 calls	109	1.16 (0.75, 1.79)		97	1.12 (0.71, 1.76)	

CI, confidence interval; OR, odds ratio

[a]Adjusted for age (continuous), sex (male, female), education (<college, college, >college), family history of thyroid cancer (yes, no), alcohol consumption (yes, no), BMI (<25, 25–29.9, ≥30 kg/m2), previous benign thyroid disease (yes, no), occupational radiation exposure (yes, no), and radiation treatment (yes, no).

Table 4.

Associations between cell phone use and risk of well-differentiated thyroid cancer by tumor size

	Tumor size ≤ 10 mm			Tumor size > 10mm		
Cell phone user	**Case**	**OR (95% CI)[a]**	**P for trend**	**Case**	**OR (95% CI)[a]**	**P for trend**
No	46	1.00		48	1.00	
Yes	166	1.06 (0.68, 1.65)		179	0.98 (0.63, 1.52)	
Hands-free device						
Yes	5	1.52 (0.47, 0.95)		3	0.68 (0.16, 2.82)	
No	161	1.05 (0.68, 1.64)		176	0.99 (0.63, 1.54)	
Daily use hour			0.116			0.485
≤1 hours/day	59	1.07 (0.63, 1.81)		60	1.05 (0.61, 1.79)	
1–2 hours/day	25	1.51 (0.78, 2.95)		31	1.26 (0.66, 2.41)	
>2 hours/day	28	1.55 (0.80, 3.03)		30	1.19 (0.62, 2.25)	
Daily phone call			0.257			0.802
≤3 calls/day	56	0.92 (0.55, 1.54)		61	0.97 (0.58, 1.61)	
3–6 calls/day	45	1.06 (0.61, 1.83)		52	0.83 (0.50, 1.40)	
>6 calls/day	51	1.32 (0.76, 2.31)		56	1.18 (0.63, 2.21)	
Phone use year			0.259			0.951
≤12 years	53	0.90 (0.53, 1.51)		71	1.03 (0.62, 1.71)	
12–15 years	64	1.04 (0.62, 1.73)		62	0.85 (0.50, 1.42)	
>15 years	46	1.33 (0.76, 2.32)		45	1.12 (0.64, 1.95)	
Age at first use			0.503			0.685
≤20 years old	19	0.63 (0.25, 1.56)		27	1.22 (0.51, 2.91)	
21–50 years old	117	0.96 (0.60, 1.56)		133	1.11 (0.68, 1.79)	
>50 years old	30	1.35 (0.71, 2.56)		19	0.72 (0.36, 1.42)	
Cumulative use hour			0.062			0.518
≤4,380 hours	36	0.97 (0.54, 1.75)		46	1.14 (0.64, 2.03)	
4,380–13140 hours	35	1.19 (0.65, 2.17)		33	0.97 (0.53, 1.79)	
>13,140 hours	40	1.75 (0.95, 3.23)		42	1.30 (0.72, 2.34)	
Cumulative phone call			0.308			0.514
≤10,220 calls	56	1.00 (0.60, 1.68)		59	1.03 (0.61, 1.72)	
10,220–41,975 calls	38	0.80 (0.45, 1.41)		58	0.93 (0.54, 1.60)	
>41,975 calls	56	1.42 (0.82, 2.46)		51	0.86 (0.49, 1.49)	

CI, confidence interval; OR, odds ratio

[a]Adjusted for age (continuous), sex (male, female), education (<college, college, >college), family history of thyroid cancer (yes, no), alcohol consumption (yes, no), BMI (<25, 25–29.9, ≥30 kg/m2), previous benign thyroid disease (yes, no), occupational radiation exposure (yes, no), and radiation treatment (yes, no).

Table 5.

Associations between cumulative cell phone use and risk of thyroid cancer by duration of cell phone use.

	Phone use ≤15 years			Phone use > 15 years		
Cell phone user	**Case**	**OR (95% CI)[a]**	**P for trend**	**Case**	**OR (95% CI)[a]**	**P for trend**
Overall						
Cumulative use hour			0.138			0.254
≤4,380 hours	85	1.07 (0.68, 1.70)		0	-	
4,380–13140 hours	42	1.07 (0.60, 1.88)		30	1.22 (0.64, 2.32)	
>13,140 hours	42	1.68 (0.92, 3.07)		45	1.42 (0.77, 2.61)	
Cumulative phone call			0.475			0.142
≤10,220 calls	109	0.98 (0.65, 1.49)		10	0.76 (0.27, 2.15)	
10,220–41,975 calls	74	0.82 (0.51, 1.32)		24	0.96 (0.48, 1.89)	
>41,975 calls	53	0.88 (0.52, 1.50)		61	1.56 (0.90, 2.70)	
Well-differentiated						
Cumulative use hour			0.139			0.349
≤4,380 hours	84	1.09 (0.69, 1.74)		0	-	
4,380–13140 hours	40	1.03 (0.58, 1.84)		28	1.14 (0.59, 2.20)	
>13,140 hours	42	1.71 (0.94, 3.12)		42	1.36 (0.73, 2.52)	
Cumulative phone call			0.488			0.228
≤10,220 calls	107	0.99 (0.65, 1.51)		10	0.77 (0.27, 2.18)	
10,220–41,975 calls	72	0.81 (0.50, 1.31)		24	0.97 (0.49, 1.92)	
>41,975 calls	53	0.90 (0.53, 1.53)		56	1.45 (0.83, 2.54)	
Papillary						
Cumulative use hour			0.244			0.354
≤4,380 hours	74	1.08 (0.67, 1.74)		0	-	
4,380–13140 hours	35	0.97 (0.53, 1.76)		24	1.11 (0.56, 2.20)	
>13,140 hours	36	1.61 (0.86, 3.01)		37	1.39 (0.72, 2.68)	
Cumulative phone call			0.412			0.260
≤10,220 calls	92	0.97 (0.63, 1.51)		9	0.91 (0.32, 2.61)	
10,220–41,975 calls	65	0.79 (0.48, 1.30)		18	0.95 (0.41, 1.77)	
>41,975 calls	47	0.86 (0.50, 1.49)		50	1.49 (0.83, 2.66)	

CI, confidence interval; OR, odds ratio

[a]Adjusted for age (continuous), sex (male, female), education (<college, college, >college), family history of thyroid cancer (yes, no), alcohol consumption (yes, no), BMI (<25, 25–29.9, ≥30 kg/m2), previous benign thyroid disease (yes, no), occupational radiation exposure (yes, no), and radiation treatment (yes, no).