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Comparison of childhood thyroid cancer prevalence among 3 areas based on external radiation dose after the Fukushima Daiichi nuclear power plant accident

The Fukushima health management survey

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Abstract

The 2011 Great East Japan Earthquake led to a subsequent nuclear accident at the Fukushima Daiichi Nuclear Power Plant. In its wake, we sought to examine the association between external radiation dose and thyroid cancer in Fukushima Prefecture. We applied a cross-sectional study design with 300,476 participants aged 18 years and younger who underwent thyroid examinations between October 2011 and June 2015. Areas within Fukushima Prefecture were divided into three groups based on individual external doses (≥1% of 5 mSv, <99% of 1 mSv/y, and the other). The odds ratios (ORs) and 95% confidence intervals of thyroid cancer for all areas, with the lowest dose area as reference, were calculated using logistic regression models adjusted for age and sex. Furthermore, the ORs of thyroid cancer for individual external doses of 1 mSv or more and 2 mSv or more, with the external dose less than 1 mSv as reference, were calculated. Prevalence of thyroid cancer for the location groups were 48/100,000 for the highest dose area, 36/100,000 for the middle dose area, and 41/100,000 for the lowest dose area. Compared with the lowest dose area, age-, and sex-adjusted ORs (95% confidence intervals) for the highest-dose and middle-dose areas were 1.49 (0.36–6.23) and 1.00 (0.67–1.50), respectively. The duration between accident and thyroid examination was not associated with thyroid cancer prevalence. There were no significant associations between individual external doses and prevalence of thyroid cancer. External radiation dose was not associated with thyroid cancer prevalence among Fukushima children within the first 4 years after the nuclear accident.

Abbreviations: CI = confidence interval, FHMS = Fukushima Health Management Survey, FNAC = fine-needle aspiration cytology, NPP = Nuclear Power Plant, OR = odds ratio, UNSCERA = United Nations Scientific Committee on the Effect of Atomic Radiation, WHO = World Health Organization.

Keywords: cancer, children, disaster, great east Japan earthquake, radiation exposure, thyroid dose

1. Introduction

The Great East Japan Earthquake struck Japan on March 11, 2011. The earthquake and subsequent tsunami hit the Fukushima Daiichi Nuclear Power Plant (NPP), causing it to release radioactive elements into the surrounding area.

One of the main adverse health consequences of radiation among exposed young people is a substantial rise in thyroid cancer rates.[1,2] To address this concern, Fukushima Prefecture started ultrasonographic examinations of the thyroid glands of its residents aged 18 years and younger 6 months after the accident.[3] Based on the preliminary results of the dose estimates, the World Health Organization (WHO) in 2013 and the United Nations Scientific Committee on the Effect of Atomic Radiation in 2015 concluded that the public health impact of radiation exposure from the incident was limited.[4,5] However, a recent study reported that residents of this age group living in Fukushima Prefecture in 2011 had approximately 30-fold excess risk of thyroid cancer compared with the national dataset of the Japanese National Cancer Center,[6] and a prevalence odds ratio (OR) compared with a reference district in Fukushima of 2.6, although this was not relative to the least contaminated area.[6]

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To clarify this inconsistency, as the responsible and practical organization of the Fukushima Health Management Survey (FHMS), we sought to examine the associations between prevalence of thyroid cancer and radiation dose, and between the prevalence and the duration from accident to thyroid examination, among Fukushima residents, on a basis of the final results of the first round thyroid examination data collected from more than 300,000 residents aged 18 years and younger. To determine the dose of radiation, we used an estimated external radiation dose based on individual behavioral data because of the limited availability of information on internal exposure to ^{131}I. Since internal exposure was closely associated with incidence of thyroid cancer among children after the Chernobyl NPP accident,[2] we further used a thyroid dose, including internal exposure, as estimated by the WHO report.[4] The authors hypothesize that there is no major geographical difference in the prevalence ratios of thyroid cancer because the dose of radiation in Fukushima was extremely lower compared with the amounts observed in the Chernobyl NPP accident.

2. Methods

2.1. Study population

Subjects were all inhabitants aged between 0 and 18 on March 11, 2011 in Fukushima Prefecture, a target population of 367,685. The first thyroid examinations were conducted from October 2011 through June 2015 as a part of the FHMS.[3] The first examinations started in 13 Evacuation Zone municipalities, then proceeded in the Nakadori (Central Fukushima), Iwaki, and Soma areas (on the Pacific coast below and above the Evacuation Zone), and the Aizu area (inland). Through April 2015, 300,476 subjects (81.7%), including evacuees currently living in other prefectures, were examined. The Ethics Committee of the Fukushima Medical University approved this study (#1318). Written informed consent was obtained from the parents of all surveyed children.

2.2. Thyroid ultrasound screening program

Ultrasonography was used for thyroid gland examinations (detailed protocol reported elsewhere).[3,7–9] Thyroid volume, nodules, cysts, and other findings, such as congenital defects and ectopic thymus were recorded. Secondary confirmatory examinations were recommended when the ultrasonography findings met the following criteria: nodules 5·1 mm or more or cysts 20.1 mm or more; or immediate need for confirmatory examination for clinical reasons. In total, 2294 participants were recommended secondary confirmatory examinations, of which 2056 (89.6%) completed them through July 2015.

The secondary confirmatory examinations included further ultrasonography, blood test, urinalysis, and fine-needle aspiration cytology (FNAC) if needed. Of 2056 participants, 537 (26.1%) underwent FNAC. Among them, 113 participants had nodules classified as suspicious or malignant and 99 participants received surgical treatment. Finally, 98 participants were diagnosed with thyroid carcinoma.

2.3. External radiation dose estimation

The Basic Survey of the FHMS for external radiation dose estimation (whose methods are detailed elsewhere)[10] was launched four months after the NPP accident. The self-administered questionnaire was prepared to collect information from all residents (n = 2,055,533) in Fukushima Prefecture concerning residence, places visited, length of time spent indoors and outdoors, and travelling time during the period from March 11 to July 11, 2011. Individual external doses were estimated by digitizing these behavior data and comparing against computations of daily gamma ray dose rate maps drawn after the NPP accident. Of all residents, 541,653 (26.4%) returned the questionnaire through June 30, 2014. The distributions of individual external doses of the respondents for the first 4 months (excluding radiation workers) were as follows: less than 1 mSv, 62.0%; less than 2 mSv, 94.0%; and less than 3 mSv, 99.4%. We used the distribution data for 59 municipalities in these analyses.[10,11] Among 541,653 participants, 129,321 participants were included in the thyroid ultrasound examination program, and individual doses were used to analyze the association between thyroid cancer and the external radiation dose.

2.4. Statistical analysis

In the present study, we consider thyroid cancer to be thyroid cancer as detected by FNAC (113 cases). After excluding one case, which was diagnosed as benign thyroid nodule after operation, there remained 112 cases for analysis.

Regarding radiation dose, we used the FHMS individual external dose distribution data.[9,10] Doses were classified into three location groups according to the distributions of doses for municipalities in Fukushima: highest dose area (≥1% of the municipality received an external radiation exposure of ≥5 mSv: 2 municipalities, Group A), middle dose area (<1% of the municipality received ≥5 mSv, <99.9% received ≤1 mSv: 39 municipalities, Group B), and lowest dose area (≥99.9% received ≤1 mSv: 18 municipalities, Group C; Fig. 1). The aforementioned 2013 WHO postdisaster health risk assessment report[4] likewise classified thyroid doses into three groups by location with a classification generally consistent with ours. Notably, the highest dose area was exactly the same as the "Group 1" defined in the WHO report.

The ORs and 95% confidence intervals (CIs) of thyroid cancer for all areas, with the lowest dose area as reference, were calculated using logistic regression models adjusted for age and sex. Furthermore, we calculated the ORs and CIs of thyroid cancer for the duration from accident to thyroid examination, and included this in the final models.

Regarding data on individual external radiation doses, the proportion of external doses of 1 mSv or more among participants with thyroid cancer was compared to that of participants without thyroid cancer. The ORs and 95% CIs of thyroid cancer for external doses of 1 mSv or more and 2 mSv or more, using an external dose of less than 1 mSv as a control reference, were calculated using logistic regression models adjusted for age and sex. SAS software (version 9.3; SAS Institute Inc., Cary, NC, USA) was used for analyses. All probability values for statistical tests were 2-tailed, with P values less than 0.05 regarded as statistically significant.

3. Results

Table 1 shows the participants' characteristics, and Fig. 2 shows the age distribution of the cases at the time of the accident as well as the age distribution at diagnosis with thyroid cancer. The number of cases increased with age, and these were similar in distribution. Table 2 shows age- and sex-adjusted ORs and 95% CIs for thyroid cancer according to location group based on the

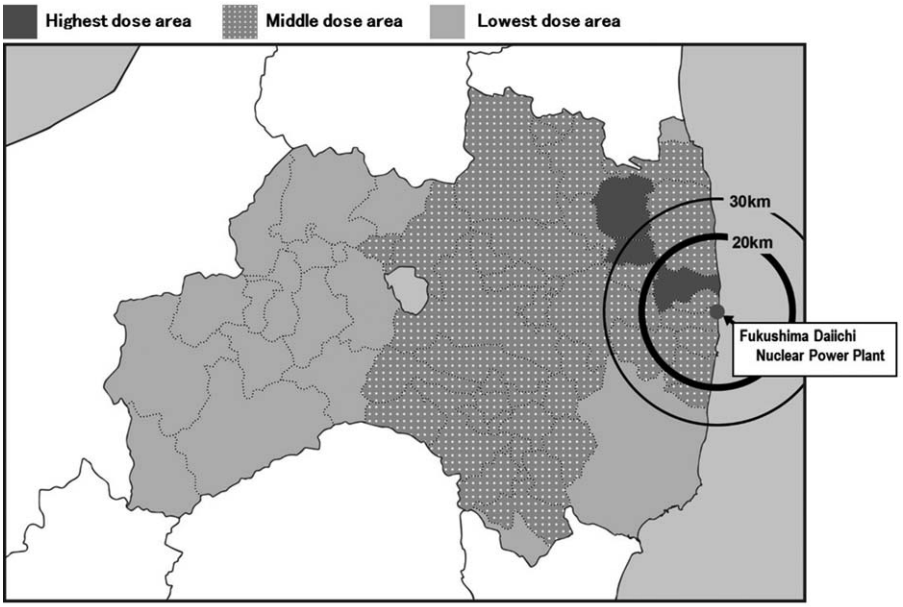

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Figure 1. Geographic details of the highest dose area, middle dose area, lowest dose area, and the Fukushima Daiichi Nuclear Power Plant.

first 4-month external radiation doses estimated by the FHMS. Prevalence of thyroid cancer for the location groups were 48/100,000 for Group A, 36/100,000 for Group B, and 41/100,000 for Group C. Compared with the lowest dose area (Group C), age- and sex-adjusted ORs (95% CIs) for Group A (the highest dose area) and Group B (the middle dose area) were 1.49 (0.36–6.23) and 1.00 (0.67–1.50), respectively. The duration from accident to thyroid examination was not associated with the prevalence of thyroid cancer. The age- and sex-adjusted OR (95% CI) of thyroid cancer for each 1-year increment of duration was 0.86 (0.68–1.08). Furthermore, we analyzed the association stratified by location group. The age- and sex-adjusted ORs (95% CI) of thyroid cancer for each 1-year increment of duration were 1.36 (0.17–11.11) for Group A, 0.84 (0.61–1.16) for Group B, and 0.70 (0.38–1.26) for Group C. We observed no interactions between radiation dose and the duration from the nuclear accident to the thyroid examination ($P > 0.20$).

When we used the first-year thyroid doses estimated by the WHO to classify location groups, the association between dose and thyroid cancer prevalence was similar to that estimated by the FHMS (Table 3). The age- and sex-adjusted ORs (95% CIs) for the highest dose (Group 1) and middle dose (Group 2) areas were 1.50 (0.37–6.15) and 1.01 (0.69–1.47), respectively.

Fifty-six cases had data on the individual external radiation dose. Of these participants with thyroid cancer, 38 (0.05%) participants had an external radiation dose <1 mSV, 17 (0.04%) had a dose of 1 mSV or more and less than 2 mSV, and 1 (0.01%) had a dose of 2 mSV ore more among 129,321 participants with external radiation dose data. When we analyzed the relationship between thyroid cancer and the individual external radiation dose, we found no significant association between them. The age and sex-adjusted ORs and 95% CIs for thyroid cancer for individual external radiation doses of 1 mSV or more and less than 2 mSV, and 2 mSV or more, with an external dose less than 1 mSV as a reference, were 0.76 (0.43–1.35) and 0.24 (0.03–1.74), respectively.

Table 1

Characteristics of the participants aged 18 years and younger in Fukushima Health Management Survey.

Characteristics	
N	300,476
Women, %	49.5
Age at the time of the nuclear accident, y (SD)	8.9 (5.1)
Age at the time of screening, y (SD)	10.8 (5.1)
Duration from the time of the nuclear accident to the time of screening, y (SD)	1.9 (0.7)
No. of cases	112
Prevalence proportion per 100,000 people	37.3

SD = standard deviation.

4. Discussion

We found that regional differences in radiation dose, as estimated by either the FHMS or WHO, were not associated with thyroid cancer prevalence among children in Fukushima in the four years after the NPP accident, and the duration from accident to thyroid examination was not associated with the prevalence of thyroid cancer in any dose area. Furthermore, there were no significant associations between the individual external radiation doses and prevalence of thyroid cancer. Along with the slow-growing nature of thyroid cancer,[12,13] these findings suggest that the prevalence of thyroid cancer in Fukushima has been influenced by factors, such as detection rate using ultrasonography,[14] other than the effects of low dose radiation exposure, and this is in line with the WHO and United Nations Scientific Committee on the Effect of Atomic Radiation reports.[4,5]

In the present study, only a few cases of thyroid cancer were diagnosed in children under 10 years old in any dose area, whereas excessive cases of thyroid cancer among younger children, especially aged between 0 and 4 years, were reported

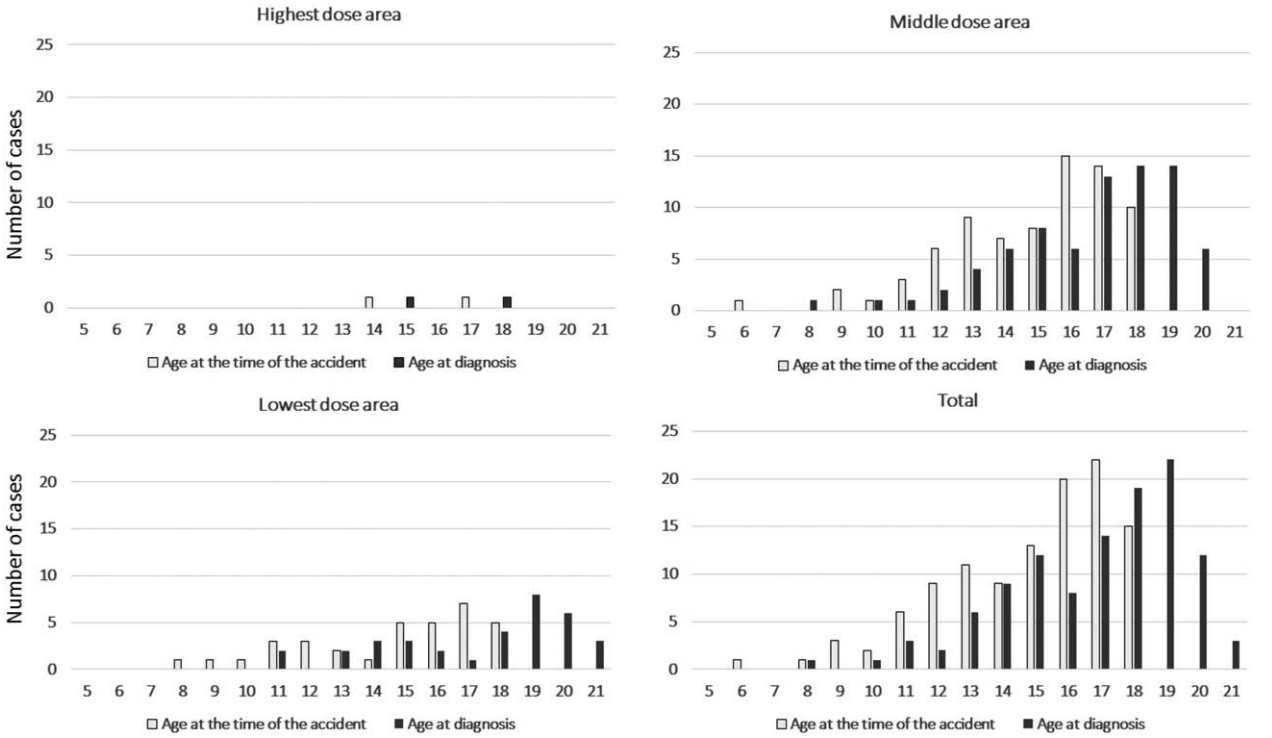

Figure 2. The age distribution of the cases at the time of the accident and the age distribution at diagnosis with thyroid cancer.

after the accident at the Chernobyl NPP in 1986,[2] which were caused by internal radiation exposure to ^{131}I through the intake of contaminated milk. The internal exposure to ^{131}I among children in Fukushima, even in the highest contaminated areas, was much smaller than that of the Chernobyl evacuees.[15,16] Although we used external radiation dose data only to examine the associations between radiation dose and thyroid cancer, the relatively highest dose area in the present study was exactly the same as that defined in the WHO report, which estimated total thyroid dose including internal exposure.[4] Although individual thyroid dose is diverse rather than external dose, area grouping might be corresponding to collective thyroid dose equivalent as well as collective external dose.

Recently, regional differences in the prevalence of thyroid cancer in Fukushima were reported[6] using interim results of the FHMS (through December 2014): the central middle district of the prefecture showed a higher prevalence OR. However, this study suffered from fundamental limitations: unsuitable geographic classifications, disregard of the slow-growing nature of thyroid cancer and its relation with radiation dose, and inappropriate statistical methods.[12,17–19] On the other hand, the observed prevalence of thyroid cancer in the present study

Table 2

Age- and sex-adjusted ORs and 95% CIs of thyroid cancer according to location group by first 4-month external radiation doses estimated by The Fukushima Health Management Survey.

	Group A*	Group B†	Group C‡
N	4,192	213,564	82,720
Women, %	50.5	49.4	49.8
Age at the time of the nuclear accident, y (SD)	9.4 (5.4)	9.0 (5.1)	8.6 (4.8)
Age at the time of screening, y (SD)	10.2 (5.4)	10.6 (5.1)	11.2 (4.9)
Duration from the time of the nuclear accident to the time of screening, y (SD)	0.8 (0.6)	1.7 (0.7)	2.6 (0.5)
No. of cases	2	76	34
Prevalence proportion per 100,000 people	47.7	35.6	41.1
Crude OR (95% CI)	1.16 (0.28–4.83)	0.87 (0.58–1.30)	Reference
Age- and sex-adjusted OR (95% CI)§	1.49 (0.36–6.23)	1.00 (0.67–1.50)	Reference
Multivariable-adjusted OR (95% CI)¶	1.01 (0.22–4.63)	0.82 (0.51–1.34)	Reference

* The group of the proportion of exposed external radiation of 5 mSv or more is more than or equal to 1%.
† The group of the proportion of exposed external radiation of 5 mSv or more is less than 1% and of 1 mSv or less is less than 99.9%.
‡ The group of the proportion of exposed external radiation of 1 mSv or less is more than or equal to 99.9%.
§ Adjusted for age at the thyroid examination and sex.
¶ Adjusted for age at the thyroid examination, sex, and duration from the nuclear accident to the thyroid examination.
95% CI = 95% confidence interval, OR = odds ratio, SD = standard deviation.

Table 3

Age- and sex-adjusted ORs and 95% CIs of thyroid cancer according to location group by first year thyroid doses estimated by WHO.

	Group 1*	Group 2†	Group 3‡
N	4,192	147,830	148,454
Women, %	50.5	49.4	49.8
Age at the time of the nuclear accident, y (SD)	9.4 (5.4)	9.1 (5.2)	8.7 (4.9)
Age at the time of screening, y (SD)	10.2 (5.4)	10.6 (5.2)	11.0 (4.9)
Duration from the time of the nuclear accident to the time of screening, y (SD)	0.8 (0.6)	1.5 (0.6)	2.3 (0.7)
No. of cases	2	52	58
Prevalence proportion per 100,000 people	47.7	35.2	39.1
Crude OR (95% CI)	1.22 (0.30–5.00)	0.90 (0.62–1.31)	Reference
Age- and sex-adjusted OR (95% CI)§	1.50 (0.37–6.15)	1.01 (0.69–1.47)	Reference
Multivariable-adjusted OR (95% CI)¶	1.07 (0.24–4.71)	0.84 (0.54–1.32)	Reference

* Relatively highest dose area.

† Middle dose area.

‡ Relatively lowest dose area classified by WHO estimation.[4]

§ Adjusted for age at the thyroid examination and sex.

¶ Adjusted for age at the thyroid examination, sex, and duration from the nuclear accident to the thyroid examination.

95% CI = 95% confidence interval, OR = odds ratio, SD = standard deviation, WHO = World Health Organization.

was higher than the expected prevalence calculated by a life-table method using the national estimates of thyroid cancer incidence rates from 2001–10.[20] The observed and estimated prevalence of thyroid cancer among residents in Fukushima aged 20 years or less was 160.1 and 5.2, respectively.[20] Although the discrepancy in the prevalence of thyroid cancer might be explained by methodological differences in detecting thyroid cancer and mass screening effects,[9] we should also carefully examine the potential for effects of radiation dose or overdiagnosis on the high prevalence of thyroid cancer in the secondary evaluation and future surveys.

The first limitation of the present study is that low exposure doses (especially compared with those at Chernobyl) and small inter-regional dose differences within Fukushima made it difficult to obtain discernible statistical results. Secondly, we did not examine confounding factors such as body mass index or dietary iodine intake.[21] Thirdly, the response rate to the questionnaire to estimate external doses in the present study was relatively low and this may affect the results, although the estimated external doses were representative of dose distribution for the whole population of each area.[22] Fourthly, the thyroid cancers observed in the present study are likely a mixture of prevalent and incident cases. This may lead to an underestimation of the association between radiation dose and thyroid cancer. However, the duration from the accident to the thyroid examination was not associated with the prevalence of thyroid cancer in any dose area in the present study. Therefore, we speculate that the incidence rate of thyroid cancer might not increase within the first four years after the NPP accident. Finally, because the mean duration from accident to diagnosis was only two years, the time may be short to expect to find radiation-related cases. The incidence of thyroid cancer in children and adolescents increased four years after the Chernobyl NPP accident,[13] although no systematic studies had been conducted within four years of the NPP accident. Therefore, in addition to the present study, follow-up surveys should be conducted for several years before any conclusions can be drawn.

In conclusion, there were no associations between the prevalence of thyroid cancer and regional and individual differences in radiation doses, or between the prevalence and the duration from accident to thyroid examination, among children in Fukushima within four years of the NPP accident. The results of a follow-up survey, which started in April 2014, should help clarify the effects of low-dose radiation exposure on the incidence of thyroid cancer in Fukushima.

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