Received: 02 June 2025 / Accepted: 02 August 2025 / Published online: 28 August 2025

DOI 10.34689/SH.2025.27.4.006

UDC 616.12-009

CURRENT STATUS OF PEDIATRIC THYROID CANCER 14 YEARS AFTER THE FUKUSHIMA NUCLEAR ACCIDENT

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Following the Fukushima Daiichi nuclear power plant accident associated with the Great East Japan Earthquake in 2011, thyroid cancers were detected through population-based ultrasound screening. We herein describe the clinicopathological features of these thyroid cancers.

The mean age at the time of the accident was 17.8 years, with a male-to-female ratio of 1:1.8. Lymph node metastasis was detected in 22.4% of cases preoperatively, but this increased to 77.6% in postoperative pathological examinations, predominantly involving peritracheal nodes. Extrathyroidal extension was observed in 39% of cases, and distant metastasis (M1) was found in 2.4%. The surgical procedures performed included total thyroidectomy in 8.8% and lobectomy in 91.2%, with lymph node dissection performed in all cases.

Histopathology revealed that 98% of cases were papillary carcinoma. Genetic analysis demonstrated BRAF mutations in 69% of cases, whereas RET/PTC3 rearrangements were rare, showing a distinct pattern compared with Chernobyl.

In summary, thyroid cancers detected in Fukushima differed significantly from those after the Chernobyl accident. Except for sex distribution, the clinical features were similar to those of both adult and pediatric sporadic thyroid cancers.

Key words: *Fukushima; thyroid cancer; radiation-induced malignancy; BRAF mutation; RET/PTC rearrangement.*

For citation:

Noso Yoshihiro Current Status of Pediatric Thyroid Cancer 14 Years After the Fukushima Nuclear Accident // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (4), pp. 44-48. *doi 10.34689/SH.2025.27.4.006*

Резюме

ТЕКУЩЕЕ СОСТОЯНИЕ РАКА ЩИТОВИДНОЙ ЖЕЛЕЗЫ У ДЕТЕЙ ЧЕРЕЗ 14 ЛЕТ ПОСЛЕ ЯДЕРНОЙ АВАРИИ НА ФУКУСИМЕ

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После аварии на атомной электростанции «Фукусима-1», связанной с Великим восточно-японским землетрясением 2011 года случаи рака щитовидной железы были выявлены с помощью ультразвукового скрининга среди населения. В данной статье мы описываем клинико-патологические особенности этих случаев рака щитовидной железы.

Средний возраст на момент аварии составлял 17,8 года, соотношение мужчин и женщин было 1:1,8. Лимфоузловые метастазы были обнаружены в 22,4% случаев до операции, но их количество увеличилось до 77,6% при послеоперационных патологических исследованиях, преимущественно затрагивая перитрахеальные узлы. В 39 % случаев наблюдалось внещитовидное распространение, а в 2,4 % — отдаленные метастазы (M1). Хирургические процедуры включали тотальную тиреоидэктомию в 8,8 % случаев и лобэктомию в 91,2 % случаев, при этом во всех случаях проводилась лимфодиссекция.

Гистопатологическое исследование показало, что в 98% случаев речь шла о папиллярной карциноме. Генетический анализ выявил мутации BRAF в 69% случаев, тогда как перестройки RET/PTC3 были редкими, что свидетельствует о наличии четкой закономерности по сравнению с Чернобылем.

Таким образом, рак щитовидной железы, выявленный в Фукусиме, значительно отличался от рака, выявленного после аварии в Чернобыле. За исключением распределения по полу, клинические особенности были схожи с особенностями спорадического рака щитовидной железы, как у взрослых, так и у детей.

Ключевые слова: Фукусима; Рак щитовидной железы; Опухоли, вызванные радиацией; BRAF мутация; RET/PTC перестройка

Для цитирования:

Носо Йошихиро Текущее состояние рака щитовидной железы у детей через 14 лет после ядерной аварии на Фукусиме // Наука и Здравоохранение. 2025. Vol.27 (4), С.44-48. *doi 10.34689/SH.2025.27.4.006*

Түйіндеме

ФУКУСИМА ЯДРОЛЫҚ АПАТЫНАН 14 ЖЫЛ ӨТКЕННЕН КЕЙІНГІ БАЛАЛАРДАҒЫ ҚАЛҚАНША БЕЗІНІҢ ҚАТЕРЛІ ІСІГІНІҢ ҚАЗІРГІ ЖАҒДАЙЫ

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2011 жылғы Ұлы Шығыс жапон жер сілкінісіне байланысты "Фукусима-1" атом электр станциясындағы апаттан кейін қалқанша безінің қатерлі ісігі аурулары халық арасында ультрадыбыстық скрининг арқылы анықталды. Бұл мақалада біз қалқанша безінің қатерлі ісігінің клиникалық және патологиялық ерекшеліктерін сипаттаймыз. Апат кезіндегі орташа жас 17,8 жасты құрады, ерлер мен әйелдердің арақатынасы 1:1,8 болды. Лимфа түйіндерінің метастаздары операцияға дейінгі жағдайлардың 22,4% - анықталды, бірақ операциядан кейінгі патологиялық зерттеулерде олардың саны 77,6% -ға дейін өсті, негізінен перитрахеальды түйіндерге әсер етті. 39% жағдайда қалқанша безден тыс таралу байқалды, ал 2,4 % - да алыс метастаздар (M1) байқалды. Хирургиялық процедураларға 8,8% жағдайда жалпы тиреоидэктомия және 91,2% жағдайда лобэктомия кірді, барлық жағдайларда лимфодиссекция жасалды. Гистопатологиялық талдау нәтижесінде 98%жағдайда папиллярлы карцинома анықталды. Генетикалық зерттеу науқастардың 69%-ында BRAF мутациясын, ал RET/PTC3 қайта құрылымдары сирек кездесетінін көрсетті. Бұл Чернобыльдегі жағдайлармен салыстырғанда айтарлықтай айырмашылықтарды көрсетеді.

Осылайша, Фукусимада анықталған қалқанша безінің қатерлі ісігі Чернобыль апатынан кейін анықталған қатерлі ісіктен айтарлықтай ерекшеленді. Жыныстық арақатынастан басқа, клиникалық ерекшеліктері ересектер мен балалар арасындағы спорадиялық қалқанша безі обырына ұқсас болды.

Түйінді сөздер: *Фукусима; Қалқанша безі обыры; радиация әсерінен туындайтын ісіктер; BRAF мутациясы; RET/PTC қайта құрылуы*

Дәйексөз үшін:

Носо Йошихиро Фукусима ядролық апатынан 14 жыл өткеннен кейінгі балалардағы қалқанша безінің қатерлі ісігінің қазіргі жағдайы // Ғылым және Денсаулық сақтау. 2025. Vol.27 (4), Б. 44-48. *doi 10.34689/SH.2025.27.4.006*

Introduction

On March 11, 2011, the Great East Japan Earthquake triggered a massive tsunami that caused a catastrophic accident at the Fukushima Daiichi Nuclear Power Plant. Large amounts of radioactive materials were released into the atmosphere, raising concerns about radiation-related health effects, particularly in Fukushima Prefecture.

In response, the national and prefectural governments launched the Fukushima Health Management Survey, which included thyroid ultrasound screening for all residents of Fukushima Prefecture who were aged 18 years or younger at the time of the accident.

This paper describes the findings from these thyroid examinations and provides an overview of the clinical outcomes observed up to the present.

Methods

Thyroid ultrasound screening of children and adolescents was initiated at the request of Fukushima Prefecture approximately eight months after the nuclear accident in 2011. The target population included about 360,000 residents who were 18 years of age or younger at the time of the accident. Follow-up examinations continued in 2015 and thereafter.

As shown in Figure 1, by three years after the accident, many high school students had moved outside Fukushima Prefecture for higher education or employment, leading to a decline in the number of examinees. Approximately 10 years after the accident, the number of participants had decreased by nearly half.

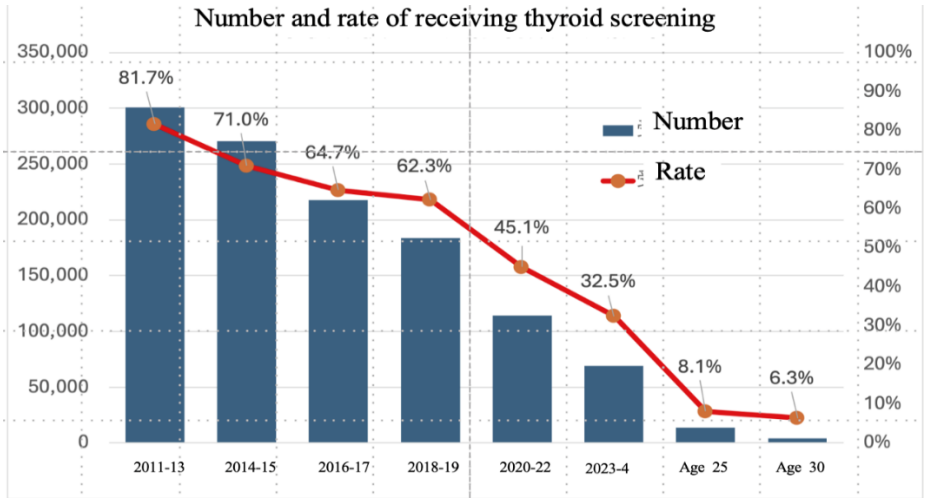

Figure 1. Number and rate of receiving thyroid screening

As summarized in Table 1, the detection of pediatric thyroid cancer gradually decreased over time, and unlike the Chernobyl nuclear accident, there was no phenomenon of a marked increase in cases beginning about three years after the event.

At the first ultrasound examination, nodules ≥5.1 mm or cysts ≥20.1 mm were referred for secondary evaluation. Secondary examinations included blood tests, urinary iodine measurement, and follow-up using established criteria [1,2]. Fine-needle aspiration cytology (FNAC) was performed when indicated, and patients were managed with either surveillance or surgery. All surgical cases underwent pathological review by an expert committee [3].

Table 1.

Trends in Detection of Pediatric Thyroid Cancer After the Fukushima Nuclear Accident.

		1st screening	2nd screening	3rd screening	4th screening	5th screening	6th screening	Screening at age 25	Screening at age 30	Total
Screening year		2011-13	2014-15	2016-17	2018-19	2020-22	2023-24	2017～	2022～	
Screened population		367,637	381,237	336,667	294,228	252,936	211,929	169,956	66,542	–
Malignant/Suspicious		116	71	31	39	50	15	26	9	357
Surgery		102	56	29	34	46	12	19	4	302
Pathology	Papillary ca.	100	55	29	34	45	12	18	4	297
	Por. diff. ca.	1	0	0	0	0	0	0	0	1
	Others	0	1	0	0	1	0	1	0	3

Between the start of the survey in 2011 and March 2021, 260 cases were diagnosed as malignant or suspected malignant, of which 219 underwent surgery. Among them, 218 cases were papillary carcinoma and 1 case was benign.

From 2011 to July 2025 (a 14-year period), 404 cases were diagnosed as malignant or suspected malignant, and 348 patients underwent surgery.

Results

Surgical Indications

In adults, treatment guidelines for thyroid carcinoma are well established. In children and adolescents, the same criteria were applied for low-risk and high-risk cases as in adults. For intermediate-risk cases, whenever possible, lobectomy with peritracheal lymph node dissection was performed, and total thyroidectomy was avoided. Postoperative outcomes were favorable in pediatric patients, and radioactive iodine (RAI) therapy was not recommended except for high-risk cases. The use of RAI in young patients was limited due to concerns from both clinicians and parents, and lifelong thyroid hormone replacement therapy after total thyroidectomy was often met with anxiety, making its implementation difficult.

Patient Characteristics

In the first detailed analysis of 125 cases, the mean age at the time of the nuclear accident was 14.8 years (range, 5–18), and the mean age at diagnosis was 17.8 years (range, 9–23).

The male-to-female ratio was 1:1.8, smaller than that observed in adult thyroid cancer [4,8].

Surgical Procedures

Total thyroidectomy was performed in 8.8% of patients, while lobectomy was performed in 91.8%.

All patients underwent lymph node dissection, with peritracheal dissection in 82.4% and lateral neck dissection in 17.6% [4,8].

Stage and TNM Classification

Stage distribution was as follows: Stage I, 97.6%; Stage II, 2.4%.

Postoperative TNM classification was pT1a 34.4%, pT1b 24.8%, pT2 1.6%, pT3 39.2%, and pT4 0%.

Lymph node status was pN0 22.4%, pN1a 60.8%, and pN1b 16.8%.

Extrathyroidal extension was observed in 39.2% (Ex1), while 60.0% had no extension.

Overall, lymph node metastasis was found in 77.6% of cases, most frequently in the central compartment (N1a, 60.8%). Microscopic extrathyroidal invasion (Ex1, corresponding to T3) was present in 39.2% of cases, which was relatively frequent.

Histopathology

The vast majority of cases were papillary carcinoma.

Among 125 reported cases, papillary carcinoma accounted for 123 cases (98.4%). Rare variants included poorly differentiated carcinoma in 1 case (0.8%), follicular variant in 4 cases (3.2%), diffuse sclerosing variant in 3 cases (2.4%), and solid variant in 2 cases (1.6%). All papillary microcarcinomas (≤10 mm) demonstrated capsular invasion.

Genetic Findings

In Chernobyl-related pediatric thyroid cancers, RET/PTC3 rearrangements were commonly observed and regarded as radiation-induced alterations. However, subsequent studies showed that such rearrangements were also frequent in non-exposed pediatric thyroid cancers, suggesting they represent a general feature of childhood thyroid carcinoma.

In Fukushima, genetic analysis was performed in 68 cases, and BRAF V600E mutations were detected in 68.3%. RET and NTRK fusions were identified in 18.5%, whereas no RAS mutations were found.

In an expanded cohort of 138 cases, BRAF V600E mutations were again common (69.6%), while RET/PTC3 was identified in only one case [11].

Table 2.

Genetic Findings

	Study 1[9], 2[10]		Study3[11]	
Mutated gene	No. of cases	%	No. of cases	%
BRAFV600E	43	68.3	96	69.6
RAS	0	0	0	0
RET/PTC1	6	8.8	8	5.8
ETV6/NTRK3	4	6.3	6	4.3
STRN/ALK	1	1.6	2	1.4
RET/PTC3	1	1.6	1	0.7
AFAP1L2/RET	1	1.6	1	0.7
PPFIBP2/RET	1	1.6	1	0.7
KIAA1217/RET	0	0	1	0.7
ΔRFP/RET	0	0	1	0.7
SQSTM1/NTRK3	1	1.6	1	0.7
TPR/NTRAK1	1	1.6	1	0.7
unknown	9*	13.2	19	13.8
Total	68	100	138	100

Thus, the genetic profile of Fukushima thyroid cancers was markedly different from the Chernobyl radiation-induced cases.

Comparison with Chernobyl

In Chernobyl, total thyroidectomy was frequently performed, followed by postoperative radioactive iodine (RAI) therapy in many cases.

Both Chernobyl and Fukushima introduced ultrasound screening programs. The distribution of tumor size was similar: T1a tumors accounted for 36.9% in Chernobyl and 35.2% in Fukushima [8,16]. In Fukushima, however, T1b tumors were more common (45.6%), likely reflecting the impact of early detection through ultrasound screening.

Regarding sex distribution, adult thyroid carcinoma in Japan occurs overwhelmingly in women [13,14]. By contrast, in Fukushima the female-to-male ratio was 1.8, and in Chernobyl it was 1.6—both considerably smaller than that seen in adult thyroid cancer.

The mean tumor diameter was 14 mm (range, 5–53 mm) in Fukushima and 15 mm (range, 2–60 mm) in Chernobyl, showing no significant difference [8,16].

Rates of clinical lymph node metastasis (cN) and extrathyroidal extension (cEx) were also similar between the two cohorts.

Distant metastasis (M1) was uncommon in Fukushima but relatively frequent in Chernobyl, where it was observed in approximately 18% of cases [13–16].

Future Perspectives

The number of thyroid cancer surgeries in Fukushima has now exceeded 300 cases. Since the accident, revisions of the Japanese guidelines for the management of thyroid cancer have complicated data interpretation to some extent.

Furthermore, many individuals who were under 18 years old at the time of the accident have since moved outside Fukushima Prefecture for university or employment. Consequently, an increasing number of patients are over 20 years of age at the time of surgery, and their treatment often diverges from the strategies originally established for younger patients. Regular postoperative surveillance has also become difficult for those living outside the prefecture, and cases of recurrence have been observed. Recurrences have been noted mainly in the contralateral thyroid lobe or in lateral lymph nodes after lobectomy, while no recurrences have been reported following total thyroidectomy. Although precise data are lacking, the recurrence rate in Fukushima is estimated to be approximately 6–7%, which is substantially lower than the previously reported rate of 20–50% [17]. In contrast, in Chernobyl, despite widespread use of total thyroidectomy and RAI therapy, recurrence was reported in 27.6% of cases, with more than half involving distant metastases [16].

In Japan, the initial treatment strategy for young patients after the accident was to avoid RAI whenever possible. However, more than a decade has now passed, and an increasing number of patients are over 20 years of age at the time of initial or recurrent disease. As a result, the number of total thyroidectomies and completion thyroidectomies performed with the intent of subsequent RAI therapy may increase in the future.

For recurrent cases with NTRK or RET gene alterations, which are often resistant to RAI, molecular targeted therapies are expected to play a key role.

Moreover, psychological care is becoming an important issue throughout the process from screening to surgery, highlighting the need for comprehensive patient support.

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