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Thyroid cancer in Ukraine after the Chernobyl accident (in the framework of the Ukraine–US Thyroid Project)

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Abstract

As a result of the accident at the Chernobyl Nuclear Power Plant, millions of residents of Belarus, Russia, and Ukraine were exposed to large doses of radioactive iodine isotopes, mainly I-131. The purpose of the Ukraine–American (UkrAm) and Belarus–American (BelAm) projects are to quantify the risks of thyroid cancer in the framework of a classical cohort study, comprising subjects who were aged under 18 years at the time of the accident, had direct measurements of thyroid I-131 radioactivity taken within two months after the accident, and were residents of three heavily contaminated northern regions of Ukraine (Zhitomir, Kiev, and Chernigov regions). Four two-year screening examination cycles were implemented from 1998 until 2007 to study the risks associated with thyroid cancer due to the iodine exposure caused during the Chernobyl accident. A standardised procedure of clinical examinations included: thyroid palpation, ultrasound examination, blood collection followed by a determination of thyroid hormone levels, urinary iodine content test, and fine-needle aspiration if required. Among the 110 cases of thyroid cancer diagnosed in UkrAm as the result of four screening examinations, 104 cases (94.5%) of papillary carcinomas, five cases (4.6%) of follicular carcinomas, and one case (0.9%) of medullary carcinoma were diagnosed.

Introduction

The US National Cancer Institute (NCI) in collaboration with the Ministries of Health of Belarus and Ukraine has initiated long-term cohort studies of thyroid diseases among the younger exposed populations in both countries. The two studies, UkrAm and BelAm are outlined in similar research protocols and are precisely designed to provide dose-specific estimates of the radiation-related risks of thyroid disease after childhood exposure to I-131 [2].

Objective and methods

Within a few weeks after the accident, direct thyroid radioactivity measurements were performed on approximately 150 000 subjects in Ukraine and about 200 000 subjects in Belarus [2]. The UkrAm group consisted of potential members who were born from 26 April 1968 to 26 April 1986 (the date of the accident), tested for thyroid activity measurements from May to June 1986 and residents residing in Chernigov, Zhitomir, or Kiev oblasts during 1986.

A sub-sample of 32 385 subjects was selected from this list and the subjects are divided in three groups based on their preliminary estimates of thyroid dose. This sub-sample included all the subjects ($N = 8752$) in the highest dose group (> 1 Gy) and a randomly selected sample from two lower-dose groups (0–0.29 and 0.30–0.99 Gy, respectively, with 15 391 and 8242 subjects, respectively). A variety of methods were used to track these subjects, who were invited from April 1998 through December 2000 to participate in the current study [2]. As a result, 13 243 (40.9%) individuals were screened for the first time between 1998 and 2000.

At the moment of the Chernobyl accident, cohort members were residing in 11 more highly contaminated areas of Chernigov, Zhitomir, and Kiev regions located within 120 km of the Chernobyl station. At the time of the accident, the residents in the 30 km zone (town of Pripyat' and the Chernobyl district) were immediately evacuated within the first days of the accident.

Each subject was screened for thyroid cancer either by a mobile team visiting the local area or at the screening centre called the Institute of Endocrinology and Metabolism in Kiev, Ukraine. The standardised screening protocol consisted of ultrasonography and palpation by an ultrasonographer and independent clinical examination and palpation by an endocrinologist. In addition, blood samples and urine samples were collected for estimating thyroid, parathyroid hormones and antithyroid antibodies, and for estimating iodine excretion respectively. A series of structured questionnaires were also administered that focused on demographic and medical characteristics and items relevant to dose estimation, such as residential history and milk consumption from May to June 1986. In addition, all subjects signed an informed consent form. An initial assessment of the presence or absence of any thyroid pathology was provided by the endocrinologist during the screening. Subjects could be referred to the Clinic at the Institute of Endocrinology in Kiev for possible fine-needle aspiration (FNA) of thyroid nodules 5 mm or more in largest dimension and thyroid surgery if required [2, 4]. At the time of first screening examinations (1998–2000), cohort members were residing mainly in three regions (Kiev, Zhitomir, and Chernigov regions).

Results

Cohort members underwent screening examinations four times (every two years) from 1998 till 2007. At the stage of cohort formation between 1998 and 2000, 13 243 subjects were screened in cycle 1 followed by three biennial thyroid examinations conducted between 2001 and May 2007 where: 12 419 subjects (93.8%) were screened in cycle 2 (2001–2); 11 745 (88.7%) in cycle 3 (2003–4); and 10 186 (76.9%) in cycle 4. A very high level of cohort 'maintenance' is evident in response rate for the fourth cycle of screening. In 2008 only in-depth examinations (FNA or thyroid surgery) were performed to study subjects who had been referred in previous cycles of active screening.

As a result of four cycles of screening examinations, 110 cohort members were operated on for a thyroid cancer: 60 from the Chernigov region, 29 from the Zhitomir region, and 21

from the Kiev region. By age at surgery, among subjects identified within the first to fourth cycles of screening there were children, adolescents, and young adults. Statistically, 96 patients were young adults aged between 19 and 36 years, 13 were adolescents aged between 15 and 18 years, and only one patient identified at the first screening was operated on at the age of 14 years (being a child).

In contrast, by age at exposure, in the majority of cases, the age of thyroid cancer patients did not exceed more than 14 years. It turned out that the age group up to 10 years was predominant among children.

The distribution of thyroid cancer cases by preliminary thyroid doses received as a result of the Chernobyl accident points out a significant predominance of patients from the high-dose group detected at the first screening. So, the crude prevalence rate per 1000 subjects screened from the low-dose group 'A' was 1.3; the middle-dose group 'B' was 3.5; and for high-dose group 'C' was 10.2, i.e. the prevalence rate of thyroid cancer cases increased with increasing exposure dose.

Among the 110 cohort members operated on for thyroid cancer from the period of 1998–2008, 45 individuals were detected at the first cycle, 32 at the second cycle, 17 at the third cycle, and 16 cases were detected by the fourth cycle of screening.

According to morphological data, most of the removed malignant tumours represented a papillary carcinoma (104 cases, or 94.5%). Follicular carcinomas (five cases, 4.5%) were diagnosed in three patients after the first screening, one patient after the second cycle, and one patient after the third cycle of screening. A medullary carcinoma was diagnosed only in one cohort member (0.9%) after the second cycle of screening. A detailed pathologic analysis of 45 carcinomas detected in first screening cycle and 11 prescreening thyroid cancer cases was published [5].

The assessment of the individual thyroid doses due to intake of I-131 for all cohort members was based on the results of direct thyroid radioactivity measurements, which yielded estimates of the I-131 activities in the thyroid at the time of the measurements and personal interviews. To calculate the thyroid dose, the variation with time of the I-131 activity was assessed using data from personal interviews (containing information on residence history, dietary habits, and individual actions taken to reduce doses) and advanced ecological models [3]. The deterministic and stochastic versions of individual dose were calculated for each subject. Individual arithmetic means of thyroid doses ranged from 0 to 40 Gy, but only 91 subjects (0.7%) had doses in excess of 10 Gy. The arithmetic mean of individual thyroid absorbed doses over the entire cohort was 0.79 Gy [3, 4].

Two dose–response analyses for the UkrAm cohort have been published up to date [4, 6]. In the cohort of 13 127 subjects screened during 1998–2000, 45 cases of thyroid cancer cases were detected. The excess relative risk per Gray (ERR/Gy) was estimated using individual doses and a linear excess relative risk model. Thyroid cancer showed a strong, monotonic, and approximately linear relationship with individual thyroid dose estimates, yielding an estimated excess relative risk of 5.25 Gy^{-1} (95% confidence interval: 1.70–27.5). In the absence of Chernobyl radiation, 11.2 thyroid cancer cases would have been expected in comparison with the 45 observed cancers.

The total of 65 cases of thyroid cancer diagnosed during the second to fourth screening cycles in 2001–7 and about 73 000 persons yr⁻¹ of observation were used in dose–response assessment of incident thyroid cancer risk [7]. The excess relative risk per Gray was estimated to be 1.91 (95% confidence interval: 0.43–6.34) and the excess absolute risk per 10⁴ person-years was estimated to be 2.21 (95% confidence interval: 0.04–5.78). The ERR/

Gy varied significantly by region of residence, but not by time since exposure. I-131-related thyroid cancer risks persisted for two decades following exposure.

Discussion and conclusions

The following conclusions from the UkrAm study can be formulated up to date.

- The crude prevalence rate of thyroid cancer per 1000 study subjects was highest at first screening examination and increased with increasing thyroid doses (1.3 in 0–0.29 Gy, 3.5 in 0.30–0.99 Gy, and 10.2 in ≥1 Gy group, respectively).
- As a result of four cycles of screening examinations from 1998 to 2008, 110 cohort members have been operated on for a thyroid cancer.
- Among 110 thyroid carcinomas detected during the four screening cycles, papillary carcinoma was predominant: 104 cases (94.5%).

The estimates of ERR/Gy for prevalent and incident thyroid cancers in the UkrAm cohort are statistically compatible with the estimates of ERR/Gy in other case–control studies of post-Chernobyl thyroid cancer [1, 9] and studies of childhood external irradiation [7]. Similarly, the estimate of excess absolute risk (EAR) in our cohort is comparable to the EARs observed in several post-Chernobyl ecological studies [1, 9]. The strengths of the current study include its prospective cohort design, using individual-measurement-based thyroid doses and uniform standardised screening for each and every subjects with the possible confounding effect of screening elimination.

The current cohort needs to be followed-up further as the radiation-related risk of thyroid cancer can persist for several decades. Future risk assessment should also incorporate the impact of individual dose uncertainties, which is in progress.

Recently published risk estimation for the BelAm cohort [8] ($n = 85$; EOR/Gy 2.15, 95% CI: 0.81–5.47) demonstrates that risk appears to be lower than in other Chernobyl studies. The epidemiological potential of the UkrAm and BelAm cohorts to further advance our knowledge of the consequences of the Chernobyl accident has been discussed recently [9].

The data obtained in the UkrAm Project demonstrate that for a period of 21 years after the Chernobyl accident thyroid cancer risks still remain reliably significant, which is a significant argument in favour of a further follow-up of cohort members of the Ukrainian–American Thyroid Project in order to ascertain the dose–effect relationship and determine the time pattern of the risk.

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