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Thyroid cancer incidence and survival among European children and adolescents (1978–1997): Report from the Automated Childhood Cancer Information System project

E. Steliarova-Foucher[a,*], C.A. Stiller[b], E. Pukkala[c], B. Lacour[d], I. Plesko[e], D.M. Parkin[f]

[a]Descriptive Epidemiology Group, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France
[b]Childhood Cancer Research Group, Department of Paediatrics, University of Oxford, Oxford, UK
[c]Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland
[d]French National Registry of Childhood Solid Tumours, Faculty of Medicine, Vandoeuvre, France
[e]Cancer Registry of Slovakia, Cancer Research Institute, Bratislava, Slovakia
[f]Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, Oxford, UK

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ABSTRACT

Data on 1690 childhood and adolescent cases of thyroid cancer registered in 61 European cancer registries were extracted from the database of the Automated Childhood Cancer Information System (ACCIS) and included in analyses of incidence and survival. In 1988–1997, the age-standardised incidence rates (ASR) for children aged 0–14 years varied in European regions from 0.5 to 1.2 per million and the age-specific incidence in adolescents aged 15–19 years ranged from 4.4 to 11.0 per million. Over the age-span 0–19 years, the female to male ratio increased from 1 to around 3. Papillary thyroid cancer accounted for almost 65% of cases in children and 77% in adolescents. In the childhood population of Belarus, the ASR for 1989–1997 was 23.6 per million and the proportion of papillary tumours was 87%. No association was found between thyroid cancer risk and national dietary iodine status across 16 countries. Incidence of thyroid carcinoma among children and adolescents in Europe (excluding Belarus) increased during 1978–1997 by 3% per year, largely due to papillary carcinoma. Survival of children and adolescents was high over the entire study period and in all regions of Europe. Children with medullary carcinoma had slightly lower 5-year survival (95%, 95% CI 81–99), than those with papillary carcinoma (99%, 95% CI 95–100). More than 90% of patients survived 20 years after diagnosis. Further standardisation of diagnostic, classification and registration criteria will be fundamental for future studies of thyroid carcinomas in young people.

1. Introduction

Thyroid cancer is rare in children, especially before the age of 10 years.[1] In European populations, the incidence rate increases steadily over the lifetime from around 1–2 cases per million in the age group 10–14 years[1] to some 70 per million at around 50 years of age, and then plateaus.[2] Cancer affecting the thyroid gland is one of few that are more frequent

* *Corresponding author:* Tel.: + 33 04 72 73 84 66; fax: +33 04 72 73 86 50.
E-mail address: steliarova@iarc.fr (E. Steliarova-Foucher).
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in females than in males, with a ratio of almost 3,[2] already seen in later childhood,[1] which may suggest the importance of hormonal factors in its aetiology.

Morphologically, four main types of thyroid carcinoma are distinguished, with different aetiology and prognosis: papillary and follicular (differentiated) carcinomas are derived from follicular cells, while medullary cancers arise from embryologically distinct C-cells. The anaplastic (undifferentiated) type is uncommon at young ages.[3]

The best known cause of thyroid carcinoma is ionising radiation, recently demonstrated by the spectacular increase in thyroid cancer incidence in the vicinity of the Chernobyl accident of 1986, especially in the childhood population.[4] At first, the increase was suspected to be largely related to opportunistic screening for these tumours and registration of non-malignant tumours. The extent of the geographical differences, however, in conjunction with the histological types of the tumours reported, removed any doubts about the reality of the association,[5] although some of the increase may still have resulted from early diagnosis of tumours that would otherwise have presented at later ages.

Exposure to radiation gives rise to differentiated types, notably to the papillary type, although a causal association for the other types cannot be excluded.[5] Medullary carcinomas are linked to hereditary factors in 25% of cases. They occur in families with multiple endocrine neoplasia (MEN) syndromes and are caused by germline mutations in the RET proto-oncogene with an autosomal dominant inheritance.[3] However, some cases of non-medullary thyroid carcinomas are also found in association with familial syndromes (e.g. adenomatous polyposis, multiple hamartomas), and their presence confers a more aggressive behaviour to these tumours.[6]

The incidence of thyroid carcinoma may also be influenced by the presence of dietary iodine (drinking water, iodised salt). Iodine deficiency has been linked with follicular carcinoma,[7] while adequate or high iodine intake may be related to higher relative frequency of papillary carcinoma.[8] Lack of dietary iodine is also associated with endemic goitre, a non-malignant disease of the thyroid gland, which may lead to the development of follicular carcinoma if specific genetic conditions are met.[9] The risk factors described above are not specific to young patients.

With the exception of the anaplastic type, thyroid carcinomas have a good prognosis. Survival of children diagnosed with thyroid cancer cases in 1978–1989 and included in the EUROCARE study was 97%[10] and similar results were also reported from the United States of America (USA).[11] These favourable figures may be partly counterbalanced by the late effects, which were reported to be more common in patients diagnosed at a young age than in adulthood.[12]

The database of the Automated Childhood Cancer Information System (ACCIS) contains records from 78 European population-based cancer registries that cover about 50% of the population aged 0–14 years and about 25% of the population aged 15–19 years living in the 35 participating countries.[13] Over the last 30 years, 1300 million person-years of observation gave rise to over 160,000 cases of childhood and adolescent cancer. The ACCIS database is particularly useful for study of rare neoplasms of children and adolescents, such as thyroid cancer. In this paper we use the ACCIS data to describe the burden of thyroid cancer in the young population of Europe in terms of incidence and survival, and propose topics for further studies.

2. Material and methods

All malignant neoplasms of the thyroid gland, registered between 1978 and 1997 in 61 European cancer registries were included in this study. The contribution of each registry, in terms of the number of cases, geographical region, calendar period, age-range of cases, method of diagnosis and follow-up for vital status is shown in Table 1. These data-sets were evaluated as 'comparable' and included in the presented analyses. Selected data quality indicators shown in Table 1 permit evaluation of each contribution. A total of 1690 cases extracted from the common ACCIS database were included in different types of analysis, as described below. Seventeen of them were second primary tumours (the second and higher primary tumours were supplied incompletely to the ACCIS database). A full account of the data collection, content of the ACCIS database and methods of its exploration is given elsewhere [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue].

For each case, the information available included basic demographic data (age, sex, country or region of residence), information on the tumour (date of incidence, site, morphology and basis of diagnosis) and on follow-up (date of last contact and vital status). Details of registration practices and data coding were provided by each registry. The population-at-risk for each registration area was supplied from official national statistics, for each sex, calendar year and age unit. Any missing population figures for combinations of calendar year, sex and age were estimated by linear interpolation of available data.

The registries were grouped into five geographical regions (British Isles, East, North, South and West). The attribution of the registries to different regions is shown in Table 1 and it was based on geographical location, combined with data availability. Because of huge differences in incidence rates of thyroid carcinoma between Belarus and the rest of Europe, the data from Belarus were excluded from the European total and presented separately. Geographical patterns of occurrence and survival were described for the period 1988–1997, which was covered by all participating registries. For the time trends analyses, the available time-span was divided into four periods of 5 years: 1978–1982, 1983–1987, 1988–1992 and 1993–1997. The registries contributing to the analyses of time trends were those contributing to at least three periods, as shown in Table 1. Table 2 shows the distribution of cases and acceptable values of the selected data quality indicators for the data-sets used in the analyses of time trends.

In this paper, the thyroid cancer is defined as in the subgroup XIb of the International Classification of Childhood Cancer (ICCC).[14] In the process of database consolidation, all tumours localised in the thyroid gland were verified in collaboration with the registries, if their original code was contained in the range M-8000 to M-8004 of the International Classification of Diseases for Oncology, second edition.[15] If applicable, such cases have received consequently more specific codes. This re-coding contributed to validity of