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Survival of children with thyroid cancer in Europe 1978–1989

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Abstract

Thyroid cancers are rare in childhood with between 0.4 and 1.5 cases per million, 2–3 times as frequent in girls as in boys. However, following the Chernobyl accident, a remarkable incidence increase was observed in children exposed to radioactive iodine fall-out. Survival after thyroid cancer in childhood is thus of interest. In the EUROCARE II study, excluding most of Eastern Europe, a total of 165 childhood thyroid cancers were reported during the period 1978–1989, of which 134 were aged 10–14 years. The childhood cancer registry in England and Wales contributed 39% of the cases, and another 24% came from the Nordic countries, the rest from other parts of west, south, east and central Europe. The 5-year survival was for both genders combined 97% (95% confidence interval (CI): 93–99), 98% (95% CI: 91–100) for boys and 97% (95% CI: 91–99) for girls, with no significant difference between the genders. Survival was high during the entire study period, and variations influenced by the small numbers. As for adults, long-term follow-up beyond 10–20 years is needed to clearly demonstrate excess mortality as a consequence of the cancer.

Keywords: Thyroid; Cancer; Child; Survival; Population-based; Cancer registries; EUROCARE

1. Introduction

Thyroid cancers are rare in childhood, and are normally not dealt with as a childhood cancer. Thyroid cancer in children and young adults however, attracted much attention following the Chernobyl accident in 1986, with an incidence increase in children exposed to radioactive iodine fall-out. The incidence reported in non-contaminated areas in Europe are in the order of 0.3–2.5 [1,2] — whereas an almost 10–15 times higher incidence was reported in Belarus in heavily contaminated areas [1] and in other Chernobyl-near areas as discussed in Ref. [3].

Three main histological groups are defined, those of follicular cell origin (papillary or follicular carcinoma) well and less differentiated, medullary carcinoma and primary thyroid lymphoma [4,5]. The papillary carcinomas are most frequently linked to radiation with a latent period ranging from 10 to 35 years. Iodine deficiency influences the type of cancer, with papillary types being more frequent in areas where dietary iodine is high.

Age, gender, histological subtype and extent of disease are known prognostic factors [6,7], with young (<50 years) having the best prognosis, and less differentiated disease and those with tumour spread at diagnosis having the poorest. None of these factors was able to be studied in the EUROCARE project [8] on adults, neither is this available from the USA-SEER publication on survival in children and adolescents (0–19 years) [9]. However, in general the 5-year relative survival is favourable in the young, being approximately 80% for European female adults (aged 14–45 years) and 99% for children and adolescents in the USA.

The aim of the present analysis was to assess the survival of children with thyroid cancer in Europe, based on the largest sample of these malignancies collected from different population-based general cancer registries and specialised population-based childhood cancer registries in central, western and northern Europe, and to create a better basis for comparison to the findings from the USA.

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2. Patients and methods

During the period 1978–1989, 165 cases of thyroid cancers in the age group 0–14 years were reported to the EUROCARE II study by the participating registries [10]. The childhood cancer registry in England and Wales, covering a population of approximately 9.6 million children, contributed 39% of the cases ($n=65$), and another 24% ($n=39$) came from the Nordic countries with a population of 2.2 million children. Only 20 cases (12%) came from the German Childhood cancer registry covering in this period only the former West Germany (child population 9.2 million), whereas 16 cases came from small populations in East European countries and 16 cases from southern Europe (Table 1).

Analyses were carried out for all histological types of thyroid cancer combined since the total number of cases was small. In addition, only meaningful analysis by gender and age-group for all countries together and for the entire time period could be performed. No age-standardised survival, nor survival using the weights of individual countries as described for the EUROCARE II [11] study could be done meaningfully due to the small number of cases.

Survival is thus given as crude observed survival rate, computed by the actuarial method [12], and stratified by age and gender.

A Cox regression analysis was carried out to study the effects of age, gender, country and period of diagnosis. Only registries from Denmark, Finland, England and Wales, Germany, Scotland and Slovakia contributing cases for the entire study period 1978–1989 were included, limiting the patients studied to 157 for the trend analysis. A detailed description of the statistical methods is given by Magnani and colleagues [13].

Table 1
Number of thyroid cancer cases 0–14 years[a] in the EUROCARE II study by participating country 1978–1989,[b] and boy–girl ratio (B/G) and age-standardised incidence per million (ASR) [2]

	Cases *n* (%)				
	Girls	Boys	Total	B/G	ASR
Northern Europe					
Iceland	–	–	–	–	0.5
Finland	13 (12)	3 (5)	16 (10)	0.2	1.3
Sweden[c]	7 (7)	3 (5)	10 (6)	0.4	1.4
Denmark	7 (7)	6 (10)	13 (8)	0.9	0.7
UK					
Scotland	5 (5)	1 (2)	6 (4)	0.2	0.5
England and Wales	43 (41)	22 (37)	65 (39)	0.5	0.5
Western and Central Europe					
The Netherlands[c]	–	–	–	–	–
Germany	9 (9)	11 (18)	20 (12)	1.2	0.4
Austria[c]	–	–	–	–	–
Switzerland[c]	1 (1)	–	1 (1)	–	1.0
France[c]	1 (1)	1 (2)	2 (1)	1.0	1.2
Southern Europe					
Spain[c]	5 (5)	1 (2)	6 (4)	0.2	1.6
Italy[c]	5 (5)	5 (8)	10 (6)	1.0	0.9
Eastern Europe					
Estonia	–	–	–	–	–
Poland[c]	2 (2)	–	2 (1)	–	0.5
Slovakia	6 (6)	7 (12)	13 (8)	1.2	0.6
Slovenia	1 (1)	–	1 (1)	–	0.4
Europe	105 (100)	60 (100)	165 (100)	0.6	–

[a] 2 cases (1%) were less than 5 years of age, 29 (18%) were 5 and 9 years and 134 (81%) were aged 10–14 years.

[b] Only Denmark, Finland, England and Wales, Scotland, Germany, Slovakia, Spain and Sweden and some registries from Italy contributed cases for the entire period 1978–1989.

[c] <20% of population covered.

3. Results

A total of 165 cases, 60 boys and 105 girls were reported during 1978–1989. Only 2 cases were reported at ages <5 years, 29 at ages 5–9 years and 134 in the age group 10–14 years. All cases, but 2, were reported as histologically confirmed, and only 6 cases had died at the end of follow-up. The number of cases by individual contributing country, the almost 2-fold higher incidence in girls compared with boys, and the age standardised incidence as reported by Parkin and coworkers [2] are presented in Table 1.

The overall 1-year survival of all cases estimated from the European pool was 99% (95% CI 96–100%), 3-year survival 99% (95–100%), and 5-year survival 97% (93–99%) (Table 2). There was no significant difference in survival between the genders. Studying survival by time since diagnosis for the only age-group with a sufficient number of cases in both genders, revealed almost no decline by time and no gender differences either (Fig. 1).

The geographical variation observed in the data for the 5-year survival is given in Table 3 along the number of cases and time period of study for each country. The Cox regression revealed no trend in survival over time (period), nor difference by any of the other variables — gender, age, country.

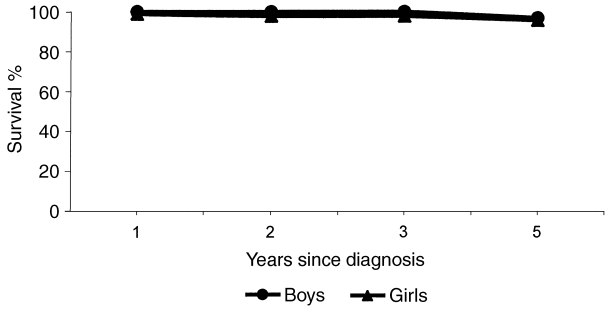

Fig. 1. Survival of children 10–14 years with thyroid cancer 1978–1989, by gender, from the EUROCARE II study.

Table 2
Thyroid cancer 1978–1989. Observed survival (Obs%) and corresponding confidence limits (95% CI) by age and gender[a]

	Age group, years			
	0–4 ($n=2$) Obs% (95% CI)	5–9 ($n=29$) Obs% (95% CI)	10–14 ($n=134$) Obs% (95% CI)	All Obs% (95% CI)
Boys ($n=60$)				
1 year	100 (34–100)	100 (82–100)	100 (91–100)	100 (94–100)
2 years	100 (34 - 100)	100 (82–100)	100 (91–100)	100 (94–100)
3 years	100 (34–100)	100 (82–100)	100 (91–100)	100 (94–100)
5 years	100 (34–100)	100 (82–100)	100 (87–100)	98 (91–100)
Girls ($n=105$)				
1 year	–	100 (74–100)	99 (94–100)	99 (94–100)
2 years	–	100 (74–100)	98 (92–99)	99 (93–99)
3 years	–	100 (74–100)	98 (92–99)	99 (93–99)
5 years	–	100 (74–100)	96 (90–99)	97 (91–99)
Overall ($n=165$)				
1 year	100 (34–100)	100 (88–100)	99 (96–100)	99 (96–100)
2 years	100 (34–100)	100 (88–100)	98 (94–100)	99 (95–100)
3 years	100 (34–100)	100 (88–100)	98 (94–100)	99 (95–100)
5 years	100 (34–100)	100 (88–100)	97 (92–99)	97 (93–99)

[a] European pooled data 1978–1989. Source: EUROCARE II study.

Table 3
Geographic variation. Thyroid cancer cases in the participating country 1978–1989 (EUROCARE II study)

	5 year survival	
	All	10–14 years
Northern Europe		
Iceland	–	–
Finland ($n=16$, 1978–1989)	100	100
Sweden[a] ($n=10$, 1978–1989)	100	100
Denmark ($n=13$, 1978–1989)	100	100
UK		
Scotland ($n=6$, 1978–1989)	83	80
England and Wales ($n=65$, 1978–1989)	98	98
Western and Central Europe		
The Netherlands[a]	–	–
Germany ($n=20$, 1978–1989)	95	93
Austria[a]	–	–
Switzerland[a] ($n=1$, 1978–1989)	100	100
France[a]	–	–
Southern Europe		
Spain[a] ($n=6$, 1985–1989)	100	100
Italy[a] ($n=8$, 1978–1989)	100	100
Eastern Europe		
Estonia	–	–
Poland[a] ($n=1$, 1978–1989)	0	0
Slovakia ($n=13$, 1978–1989)	100	100
Slovenia ($n=1$, 1985–1989)	100	100
European pool	97	97

[a] $<20\%$ of population covered.

4. Discussion

The incidence of thyroid cancer in Europe based on the present material gives similar levels to those reported in the literature, and the boy/girl ratio with a more than 2-fold higher incidence in girls is also confirmed, with a few exceptions (Table 1). The age distribution in our material also compared well with other published data [2,5,9]. The geographical survival variations within Europe could not be assessed due to small numbers. However, the low number of cases from West Germany is noteworthy, as is the apparent drop in incidence in East Germany, from being comparable to the Nordic countries, to levels similar to those of the former Federal Republic included in our study [2]. This indicates that registration methods may have a significant impact on part of our data which may be selected in an unknown way. The German childhood cancer registry rely on the close collaboration with paediatric oncologists, who rarely treat thyroid cancer (data not shown), and hence these cancers are expected to be under reported in comparison to general registration systems seen elsewhere like the Nordic countries and the UK. A similar general registration system was operating in the past in the DDR (East Germany), whereas today, like in West Germany, 'informed consent' to registration applies. Less than 1% of West German parents refuse registration (data not shown) so for childhood thyroid cancer the possible bias of the survival estimates due to this may be small.

Similar incidence figures as seen in our combined data were reported in the SEER programme [9]. This is contrary to the reports from the Chernobyl-afflicted children in Belarus, Ukraine and certain oblasts in Russia, where more than 300–400 new cases have been observed in children aged below 14 years at the time of the accident [3]. Inspecting numbers from Belarus in Cancer Incidence in Five Continents 1988–1992, a total of 151 new cases occurred in a population half the size of the Nordic countries where 23 cases appeared during the same years, and this was even more marked when comparisons with the SEER — white group were made, where only 35 cases occurred. Although some 'screening effect' in the afflicted children can not be ruled out, the incidence increase is now accepted as true. In addition, some 'screening effects' due to awareness after the accident may be present in the rest of Europe, and evidently cases found by active diagnostic measures may have a different and likely better survival than other cases.

The present data does not allow any in-depth analysis of survival. However, some conclusions might be warranted. The survival following thyroid cancer is favourable for children and 5 years after diagnosis close to 100%. This was also seen in children and adolescents in the USA [9] and in the youngest age group in the EUROCARE II analysis for adults [10], where the survival for the age-group 15–44 years and both genders combined is 95%. However, the literature points to the fact that survival following thyroid cancer should be followed for decades, in particular since relapse rates and metastasis in the very young (< 10 years) are higher than those seen among adults [4].

The EUROCARE database thus may, if maintained and updated in the coming decades, also shed light on excess mortality in children diagnosed with a rare cancer such as thyroid. It may also in time allow analysis by histological subgroups. However, this was not even possible among the adults where more than 1000 cases were accumulated in the age-stratum 15–44 years. In contrast, the time trend for survival for this age-group from 1978 to 1989 showed no change in the survival which remained high throughout the entire period — as was also seen in our data, where available, for the children.

5. The EUROCARE Working Group for this study

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