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Original Paper

Variation in Survival of Adult Patients with Thyroid Cancer in Europe

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The survival of patients with thyroid cancer was analysed using population-based EUROCARE II data from 1978–1989 (trends in survival) and 1985–1989 (cross-sectional comparisons between areas). The data consisted of 7504 patients and covered 37 cancer registration areas in 17 European countries. In 90% of the patients the diagnosis was histologically confirmed. The prognosis of patients with thyroid cancer was relatively favourable. The overall 5-year relative survival rate was 72% for men and 80% for women. Substantial variation in this 5-year rate was observed between countries ranging from 59 to 83% in men and from 72 to 84% in women. Higher than average survival rates were observed in Finland, Iceland, The Netherlands and Sweden. Countries with lower than average rates were Denmark, England, Estonia, Slovakia, Slovenia and Poland (women). Elderly patients had lower survival rates than the younger ones. Time trends in survival (which could be analysed only in selected countries with sufficient numbers of cases) were irregular but generally showed slight increases compared with rates in 1978–1980. Different distributions in the histological subtypes of thyroid cancer is one plausible explanation for the variation in the survival rate. Other likely factors contributing to this are differences in the stage distribution and varying efficacy of treatment. The EUROCARE II data did not permit specific analyses of the roles of various prognostic factors. © **1998 Elsevier Science Ltd. All rights reserved.**

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INTRODUCTION

CANCER OF the thyroid is characterised by a higher incidence rate in women than in men [1] and by wide variation in survival rates depending on the histological type of the tumour [2–4]. Other known prognostic factors include the stage of the disease and age of the patient. In this study, variation in survival within Europe of adult patients with thyroid cancer from 1985–1989 is described on the basis of data from the EUROCARE II study. Since thyroid cancer was not included in the first EUROCARE monograph [5], this is the first report on the survival of thyroid cancer patients across Europe from this dataset.

PATIENTS AND METHODS

In the EUROCARE II study, 45 cancer registries in 17 countries submitted data for centralised analysis. In this study, all malignant tumours of the thyroid (except lymphomas) in patients aged 15 year or more were included. There were 7504 cases (Table 1). Of these, 90% were histologically confirmed, ranging from 76% (England) to 100% (Switzerland). The proportion of death certificate only (DCO) cases varied from 0 to 6% between the countries, but these were excluded from the survival analysis. In general, some 25–40% of the cases were aged 65 years or more (Table 2). Data covered the entire population for Denmark, Estonia, Finland, Iceland, Scotland, Slovakia and Slovenia; in the other countries, the coverage varied between 2 and 50% of the population.

Variation in survival within Europe was analysed using data from 1985–1989, although in some regional registries (contributing to the data for the given country) the period was less than 5 years. Trend analyses were performed for the

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Table 1. *Data quality for adult patients (*15 + *years of age) with thyroid cancer,* 1985–1989 *(EUROCARE* II*)*

Country	% Coverage	No. of cases	% > 65 years	% DCO	% HV
Northern Europe					
Iceland	100	81	28	0	85
Finland	100	1156	26	0	99
Sweden*	17	427	38	0	96
Denmark	100	482	41	0	98
U.K.					
Scotland	100	473	36	1	91
England	50	1933	37	4	76
Western and Central Europe					
The Netherlands*	6	96	31	NA	97
Germany*	2	189	35	4	95
Austria*	8	73	36	5	94
Switzerland*	6	64	26	0	100
France*	5	230	23	NA	98
Southern Europe					
Spain*	10	342	26	2	97
Italy*	10	937	24	1	88
Eastern Europe					
Slovenia	100	237	30	1	96
Slovakia	100	465	32	6	91
Poland*	6	135	33	1	88
Estonia	100	184	38	1	95
Europe		7504	32	2	90

* < 20% of the national population covered. NA, not available. HV, histologically verified.

12-year period of 1978–1989. If the gender-specific number of cases was less than 50 for a particular country, the corresponding survival rate is not presented. If one or more of the gender and age-specific numbers of cases was less than 15, the gender-area combination was excluded from the age analysis. Due to small numbers of cases (and irregularities in the time periods covered), no age-specific rates are presented for Austria, Poland and Spain. Similarly, results are not given for men in Estonia, The Netherlands and Switzerland. However, all cases were included in the calculation of survival rates for Europe as a whole.

The survival rates are presented separately for men and women and for five age groups. The proportions of the main histological types of thyroid cancer (papillary carcinoma, follicular carcinoma, other specified histology, unspecified or no histology) available in the EUROCARE database were taken into account only to explain variation by country in the survival rates. Relative 1- and 5-year survival rates were used as measures of survival [6].

The European survival rates were calculated as weighted averages, the weights being the numbers of cases of thyroid cancer in the country in 1985–1989; for countries with incomplete coverage of the population, these numbers were estimated. Country-specific survival rates were age-standardised using the age distribution of the EUROCARE site-specific data as a reference.

RESULTS

Intercountry differences in survival

Overall, between 1985 and 1989, the 1-year age-standardised relative survival rate of thyroid cancer patients was 77% for men and 83% for women. The corresponding 5-year relative survival rates were slightly lower, at 67% for men and 78% for women (Figure 1). Thus, thyroid cancer has a relatively favourable outcome compared with other malignant tumours. The country-specific age-standardised 5-year relative survival rates showed substantial variation ranging from 56% (Slovenia) to 88% (Iceland) in men and from 66% (Poland) to 90% (Iceland) and 100% (Austria) in women (Figure 1). Registry-specific survival rates were available from England, France and Italy. The variation observed was of the same order as that between countries (data not shown) [7].

The effect of age on survival

In general, the 5-year relative survival rate was highest amongst young patients (Table 3). In the age group 15–44 years, for men the rate was at least 86% and for women at least 94%. In contrast, much lower rates and substantial intercountry variation were seen among the two oldest age groups (65–74 and 75 + years) in both genders.

Time trends in survival

Due to the small number of age-specific cases, time trends in the 5-year relative survival rate were calculated for selected countries only (Table 4). Marked irregularities were noted. For men, survival improved with time in Denmark, Sweden and Scotland, whereas in Finland, England and Italy survival was largely unchanged. For women, a consistent but slight increase in the 5-year relative survival rate was seen only in Scotland.

The effect of histological type of tumour on survival

Specific survival rates for each histological type of tumour were not calculated in this study. However, there was marked variation in the distribution of types of thyroid cancers between countries. Due to differences in patient survival between the two main histological types of thyroid cancer, i.e. papillary carcinoma (with a very favourable prognosis) and

follicular carcinoma (with lower survival rates) [8, 9], the variation in the ratio of the numbers of cases with papillary and follicular carcinomas could explain at least some of the survival differences between the countries. This ratio for all patients was as high as 4.2 in Iceland, 2.9 in Switzerland and 2.6 in Italy but only 0.6 in Estonia and 1.0 in The Netherlands; in most other countries there were somewhat more papillary carcinomas than follicular carcinomas (the range of the ratio for these countries was 1.1–1.8) which is the predominant pattern reported from both clinical and cancer registry studies in the Western world [3, 10].

Table 2. Numbers of adult patients (15+ years of age) with thyroid cancer, 1985–1989, by country, gender and age (EUROCARE II)

Country	Age group (years) 15–44	45–54	55–64	65–74	75+	Total
(a) Men						
Northern Europe						
Iceland	8	6	9	4	4	31
Finland	85	43	42	42	21	233
Sweden*	42	25	23	30	20	140
Denmark	33	25	23	35	25	141
U.K.						
Scotland	40	22	23	20	17	122
England	144	82	128	132	78	564
Western and Central Europe						
The Netherlands*	6	7	6	3	1	23
Germany*	17	12	10	11	4	54
Austria*	4	4	3	3	2	16
Switzerland*	2	4	4	3	-	13
France*	23	13	10	8	1	55
Southern Europe						
Spain*	30	9	13	11	12	75
Italy*	88	40	60	36	20	244
Eastern Europe						
Slovenia	22	10	10	14	9	65
Slovakia	31	16	21	18	13	99
Poland*	4	1	12	3	2	22
Estonia	6	6	6	4	3	25
Europe	585 (30%)	325 (17%)	403 (21%)	377 (20%)	232 (12%)	1922
(b) Women						
Northern Europe						
Iceland	23	6	6	6	9	50
Finland	404	164	123	119	113	923
Sweden*	87	41	46	66	47	287
Denmark	111	48	44	63	75	341
U.K.						
Scotland	116	54	49	63	69	351
England	462	195	205	232	275	1369
Western and Central Europe						
The Netherlands*	29	8	10	13	13	73
Germany*	37	22	24	33	19	135
Austria*	19	11	6	12	9	57
Switzerland*	26	4	6	7	8	51
France*	78	26	26	25	20	175
Southern Europe						
Spain*	110	46	46	44	21	267
Italy*	279	133	111	98	72	693
Eastern Europe						
Slovenia	50	29	44	29	20	172
Slovakia	124	64	60	61	57	366
Poland*	33	20	20	20	20	113
Estonia	47	23	27	30	32	159
Europe	2,035 (36%)	894 (16%)	853 (15%)	921 (16%)	879 (16%)	5582

* < 20% of the national population covered.

DISCUSSION

The outcome of patients with thyroid cancer is one of the best amongst all cancers and thus, the rates, on average, are much higher than those for other cancer patients. Substantial

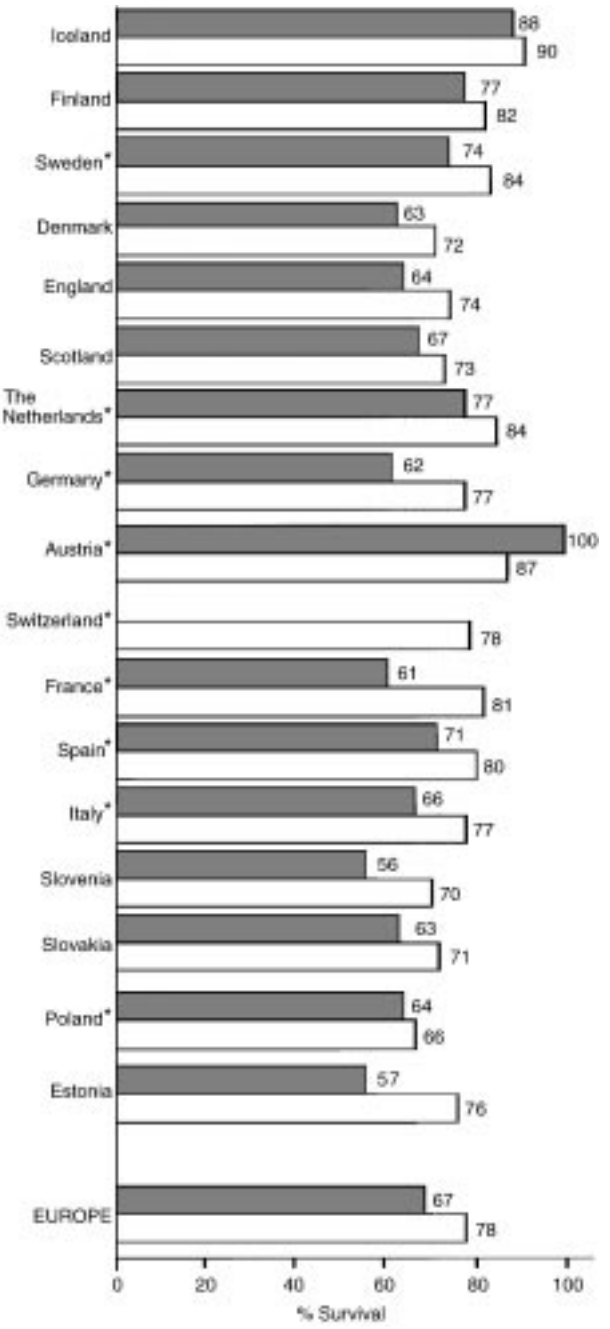

Figure 1. Relative 5-year survival rates (age-standardised) of adult patients (15+ years of age) with thyroid cancer in 1985–1989, by country and gender (EUROCARE II). □ women, ■ men. * < 20% of the national population covered.

Table 3. The relative 5-year survival rates (%) of adult patients (15+ years of age) with thyroid cancer diagnosed in 1985–1989, by country, gender and age (EUROCARE II)

Country	Age group (years)					Total
	15–44	45–54	55–64	65–74	75+	
Men						
Denmark	86	46	48	44	66	59
Finland	97	94	71	66	29	83
Sweden*	86	95	84	69	17	78
Scotland	99	90	54	33	23	72
England	92	66	63	37	32	64
Italy*	93	84	57	44	17	72
Europe	93	80	63	48	20	72
Women						
Denmark	96	85	72	53	20	72
Finland	99	97	86	66	43	88
Sweden*	97	96	86	71	51	84
Scotland	98	87	70	53	22	74
England	98	93	70	50	32	75
France	97	81	91	56	61	85
Italy*	99	94	80	50	35	83
Estonia	94	89	71	61	42	76
Slovakia	96	90	68	43	29	75
Slovenia	95	85	65	36	42	72
Europe	98	88	76	58	42	80

* < 20% of the national population covered.

variation was observed in survival between the countries for both men and women—demonstration of this variation was the main object of the present study. Clearly higher than average survival rates were found in Finland, Iceland and The Netherlands and in the area covered by the registry in Sweden. Countries with a lower than average survival were Denmark, England, Estonia, Scotland, Slovakia and Slovenia and the area covered by the registry in Germany. Due to possible selection problems (e.g. in terms of standard of living and cancer care in the area), direct comparisons of the survival rates between countries in which the participating cancer registries cover the whole population or a large part of it, and those represented by few regional registries covering only a fraction of the population must be made with caution.

Because of the variation in the periods covered and differences in the methodology used in calculating survival rates (e.g. different weights in standardisation), no straightforward comparisons are justified between the current EUROCARE survival data and those obtained in earlier population-based survival studies in other countries. However, the relatively favourable outcome of patients with thyroid cancer found in this study is, in general, in accordance with the results of many earlier reports from The Netherlands [11], Scotland [12], Slovenia [13] and Sweden (countrywide material) [14].

There are no simple ways to assess the role of different causes of the variation in the survival of patients with thyroid cancer in Europe. Severe patient selection is an improbable cause because the patient data originated in population-based cancer registries. Differences in the age distribution of the patients were largely eliminated by age-standardisation of the rates. The differences in the diagnostic delay (leading to different stage distributions) and variation in the effectiveness of treatment are, of course, important factors but their role can only be evaluated in specific studies.

Table 4. The relative 5-year survival rates (%) of adult patients (15+ years of age) with thyroid cancer in four consecutive 3-year periods in 1978–1989 in selected countries, by gender (EUROCARE II)

Country	1978–1980	1981–1983	1984–1986	1987–1989
Men				
Denmark	50	52	55	64
Finland	71	75	73	71
Sweden*	56	66	66	84
Scotland	49	64	65	67
England	59	64	60	63
Italy*	45	64	56	47
Women				
Denmark	65	69	71	68
Finland	79	79	78	82
Sweden*	73	84	77	87
Scotland	65	69	71	72
England	66	70	72	71
Italy*	73	79	75	76

* < 20% of the national population covered.

Some of the variation in survival could be attributable to different distributions of histological types. One reason for not calculating specific survival rates for each histological type was the uncertain quality of data on histological types in the EUROCARE database. There may be inconsistencies in the original classification of the tissue specimens by the pathologists (which can only be overcome by reclassification of the tumours), but problems also arose in the interpretation of the registry-specific histology codes at the EUROCARE analysis centre. Furthermore, the registration and coding practices of all the individual cancer registries were not known in terms of occult papillary carcinoma of the thyroid with excellent prognosis (coded as *in situ* type lesion or ordinary cancer). Their inclusion in the data analysed in this study would improve the survival rate estimate, and differences in the inclusion criteria between countries would cause difficulties in the comparison of the rates.

It can be hypothesised that if the proportion of papillary carcinomas in a given country is high, the survival rate would also be higher than in countries with a lower proportion. In fact, Iceland and Switzerland did have a high ratio of papillary/follicular carcinomas (P/F) and also higher than average survival rates. However, the same pattern did not always hold true, for example, for The Netherlands (low P/F but high survival rate). Because of the apparent uncertainties in the histology codes in the EUROCARE database, no formal analyses were made on the role of the histological patterns in explaining the variation in the survival of thyroid cancer patients between the countries. This would require a specific study in which histopathological reclassification of the tumours should occupy a central position [15]. It is well known that the histological pattern of thyroid cancer varies between different age groups, papillary carcinoma being the predominant type among younger age groups and anaplastic carcinoma (associated with poor prognosis) occurring mainly in elderly individuals [4]. Thus, histology is probably the most important factor in explaining the large variation by age in the survival rates of patients with thyroid cancer in this EUROCARE study. This does not, however, explain the large intercountry variation in survival rates in older age groups. In addition to a small number of cases, the

differences in the stage distribution could well be an explanation. Most papillary carcinomas are localised and, thus, relatively easy to treat (and even tumours with regional lymph node metastases have a favourable behaviour) which is compatible with only slight intercountry variation in the survival in younger age groups. In contrast, for elderly patients one can assume that there is wide variation in the stage distribution of cancers which would result in wide variation in the survival rate.

In many studies, the proportion of papillary carcinoma in women has been higher than that in men [4, 10]. This probably contributes to the observed gender difference in the survival of patients with thyroid cancer, with women having consistently higher rates.

The variation within Europe in the survival rates of patients with thyroid cancer is similar to that found for many other cancers, with certain countries characterised by higher than average (or lower than average) survival rates for most cancer types. This means that prognostic factors specific for thyroid cancer do not necessarily explain the observed differences in country-specific survival rates.

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APPENDIX

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