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Original Paper

Variation in Survival for Adults with Nasopharyngeal Cancer in Europe, 1978–1989

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During the period 1978–1989, 2,054 new patients with nasopharyngeal carcinoma (NPC) were registered in the EUROCARE study, which, during 1985–1989 involved 45 population-based cancer registries in 17 countries. The follow-up time was at least 5 years. 48% of all cases were squamous cell carcinomas and 39% undifferentiated carcinomas, which were more frequent in males. The overall relative 1- and 5-year survival rates (data included from 8 countries with complete data) were 75 and 34%, respectively, for males, and 72 and 32%, respectively, for females, but in a multivariate analysis, there was no significant difference in risk between males and females (0.93 (0.84–1.01), hazard ratio (HR) with 95% confidence interval (95% CI) for females). The overall relative 5-year survival (data included from nine countries with complete data) declined with age, from 53% for patients aged 15–44 years to 31% for patients aged 65–74 years. For patients with undifferentiated tumours, higher survival rates were observed in Scandinavia, Slovakia and Mediterranean countries, with lower rates for patients from the U.K. and Estonia. Survival for patients with squamous cell carcinoma was lowest in Scotland, England and Estonia. In a multivariate analysis, there was a significant difference in risk of death between those with squamous cell carcinomas and those with undifferentiated (HR 0.82, 95% CI 0.74–0.90). Between 1978 and 1989, the prognosis did not change. © **1998 Elsevier Science Ltd. All rights reserved.**

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INTRODUCTION

NASOPHARYNGEAL CARCINOMA (NPC) is common in some East-Asian and Northern African countries, but rare in Europe [1]. In southern China, with incidence rates of 15–40 per 100 000 person years, the reported 5-year survival rates vary from 20–48% [2, 3], whilst a figure of 43% has been reported from Japan [4]. Patients with the undifferentiated cell type have a better 5-year survival rate than those with squamous cell tumours [5]. These two tumours usually comprise more than 80% of all patients. American patients of Chinese ethnicity have a better survival from NPC than caucasians [6, 7].

Nasopharyngeal carcinoma is uncommon in Europe, the incidence rates in most populations being below 1 per 100 000 person years [1]. Between 1978 and 1985 the pooled relative 5-year survival rate in the EUROCARE study, carried out in almost 30 cancer registries in 10 European countries was approximately 38%, varying from 54% between the ages of 15–44 years to 30% in patients over the age of 75 years [8]. Variation in relative survival between countries seemed to be present, but was difficult to interpret due to low numbers of patients. Since 1996, almost 3.5 million patients newly diagnosed with cancer in 17 European countries during the period 1978–1992 and recorded in 45 population-based cancer registries have now been included in the EUROCARE database. Therefore, this database may be particularly useful for specific analyses of rare tumours, especially for subdivided analysis according to morphology. NPC comprises less than

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Table 1. *Data quality by country for nasopharyngeal cancer,* 1985–1989 *(EUROCARE* II*)*

	Patient numbers	% DCO	% HV	% Undifferentiated carcinoma	% 15–54 years of age	% Lost to follow-up
Northern Europe						
Iceland	4					
Finland	66	0	97	20	35	0
Sweden*	36	0	100	–	35	0
Denmark	116	0	100	33	30	0
U.K.						
Scotland	96	3.1	88	–	38	0
England	449	3.6	78	42	35	0
Western and Central Europe						
The Netherlands*	12†					
Germany*	34	0	100	–	55	0
Austria*	5†					
Switzerland*	8†					
France*	38	0	100	40	45	5.3
Southern Europe						
Spain*	118	2.5	95	56	55	2.5
Italy*	180	1.7	89	40	25	1.1
Eastern Europe						
Slovenia	44	0	100	33	46	0
Slovakia	123	3.3	95	–	53	0
Poland*	24	0	96	33	30	4.2
Estonia	36	0	97	71	45	0
Europe	1389	2.1	90	39	35	0.5

* < 20% of the national population covered. †Other data not provided due to small numbers. DCO, Death certificates only; HV, histologically verified.

1% of all the tumours in the EUROCARE database [9], but an analysis of histological types within the EUROCIM database indicated that valuable prognostic data are obtainable [10]. Therefore, an analysis of survival according to histology for 1978–1989 was calculated using the EUROCARE database, and in addition we also performed a multivariate analysis of various prognostic factors, except stage at diagnosis for which data were insufficient.

PATIENTS AND METHODS

Data on patients with a first cancer diagnosis of NPC were derived from the EUROCARE study for the period 1978–1989. 2,054 adult patients were diagnosed in 17 European countries and recorded in up to 37 registries, covering approximately 15% of all patients in Europe. In eight countries the registry coverage was less than 20%. The patients were followed for at least 5 years. An overview of the quality of the data according to country for the period 1985–1989 ($n = 1{,}389$) is presented in Table 1: the histological verification rate was generally over 95%, except in the U.K. and Italy. A small group of patients with a diagnosis at autopsy ($n = 7$) and registered by death certificate only ($n = 29$) was excluded from the analysis of survival. The percentage patients lost to follow-up was also small. Due to no cases in some age-specific stata, data from registries in southern Sweden and The Netherlands, Germany, Switzerland, Poland and Estonia were excluded from comparative age-standardised survival analysis for the period 1985–1989. The age-specific analysis was carried out on cases diagnosed between 1978 and 1989 for a limited number of participating registries; data are only shown for age groups 15–44, 55–64 and 65–74 years.

The analysis according to histological subtype used the International Classification of Disease-Oncology (ICD-O): squamous cell carcinoma comprised the codes 8050–8081; lymphoepithelioma (8082) and unspecified morphology (8001–8034) were considered as undifferentiated cell type and sarcoma consisted of the codes 8800–8933, 8990–8991, 9020–9044, 9120–9134, 9141–9340 and 9540–9581.

Table 2. *Relative* 1- *and* 5*-year age-standardised survival (%) of patients with nasopharyngeal cancer in* 8 *countries of Europe,* 1985–1989§ *(EUROCARE* II*)*

	Men		Women	
	% 1 year (SEM)	% 5 year (SEM)	% 1 year (SEM)	% 5 year (SEM)
Northern Europe				
Finland	88 (4.9)	45 (8)	75 (7)	36 (6.5)
Denmark	69 (4.6)	37 (5.1)	76 (7.8)	28 (6)
U.K.				
Scotland	71 (4.7)	27 (4.5)	34 (6.6)	17 (5)
England	68 (2.8)	35 (3.4)	69 (3.9)	37 (4)
Southern Europe				
Spain*	72 (5.9)	29 (4.8)	76 (7)	no data
Italy*	77 (4.7)	34 (3.9)	78 (7.6)	42 (6.8)
Eastern Europe				
Slovakia	61 (6.6)	34 (5.8)	55 (7.7)	no data
Estonia	72 (7.6)	27 (6.3)	86 (12)	27 (4.3)
Europe†	75 (2.5)	34 (2.8)	72 (3)	32 (4.4)
Trimmed range‡	68–77	27–37	55–78	27–42
% of mean	13	33	34	50

* < 20% of the national population covered. †Weighted pool of age-standardised rates. ‡After exclusion of extreme values. §Countries were excluded if there were no cases in specific age groups. SEM, Standard error of the mean.

Table 3. 1 *and* 5*-year age-specific crude survival (%) of patients with nasopharyngeal cancer diagnosed in adults in* 9 *European countries* (1978–1989)† *(EUROCARE* II*)*

Country	15–44 years		55–64 years		65–74 years	
	1 year % (SEM)	5 year % (SEM)	1 year % (SEM)	5 year % (SEM)	1 year % (SEM)	5 year % (SEM)
Northern Europe						
Finland	89 (4.3)	56 (7.2)	75 (6.4)	53 (7.5)	56 (6.9)	27 (6.2)
Sweden*	88 (6.5)	67 (9.4)	70 (8.3)	41 (9.1)	67 (8.4)	42 (8.9)
Denmark	87 (4.8)	54 (7.4)	74 (4.9)	36 (5.4)	61 (4.8)	21 (4.2)
U.K.						
Scotland	77 (5.8)	31 (7.1)	54 (5.5)	14 (4.0)	50 (5.7)	20 (4.7)
England	82 (2.8)	53 (3.8)	63 (3.2)	30 (3.1)	53 (3.1)	21 (2.6)
Southern Europe						
Spain*	82 (6.7)	36 (8.7)	75 (7.7)	28 (9.3)	52 (11)	
Italy*	90 (4.2)	56 (7.0)	74 (4.9)	26 (4.9)	49 (6.9)	23 (5.8)
Eastern Europe						
Slovakia	78 (4.5)	54 (5.7)	68 (5.5)	29 (5.3)	59 (6.4)	25 (5.8)
Estonia	81 (9.8)	48 (13)	65 (9.9)	25 (9.2)	53 (12)	16 (9.5)
Europe‡	83	53	79	27	69	31
%Trimmed range‡	78–89	36–56	63–75	25–41	52–61	16–27
% of Europe§	14	40	19	50	17	50

* < 20% of the national population covered. †Only 15 countries participated between 1978–1989, of which only 9 had sufficient data for this analysis. ‡$P < 0.01$, log rank trend test for age at diagnosis. §After exclusion of extreme values. SEM, standard error of the mean.

Relative survival (the ratio of crude and expected survival, based on general mortality rates) was computed with the program of Hakulinen [11]. Variability was expressed by calculation of the standard error of the mean (SEM) according to Greenwood [12]. Histology-specific crude survival analysis was carried out according to country by means of Kaplan–Meier estimates because data of expected mortality were not available. To estimate variation between countries, a trimmed range was calculated after exclusion of extreme values at both ends and divided by the European figure. To estimate the hazard of death, a multivariate analysis was carried out by means of Cox proportional regression, controlling for age, histological type, gender and period of diagnosis [13]. Data on stage were not used because they were only available in a few registries.

RESULTS

Inter-country differences in survival

Of the 2,054 NPC cases that occurred during the period 1978–1989, 67% were men and 33% women; 73% had died at the end of the follow-up. On average 48% of all cases were of squamous cell carcinomas, 39% were undifferentiated and 12% were sarcomas or other cell types. The percentage of undifferentiated tumours varied for men and women from over 50% in southern countries to up to 30% in Scandinavia. The percentage of patients below 55 years of age varied from 10% in Denmark to 30% in Spain and Slovakia. Between 1985–1989, the overall relative 1- and 5-year survival rates for eight countries were 75 and 34%, respectively, for men and 72 and 32%, respectively, for women (Table 2). Five-year relative survival was slightly higher for men in Scandinavia; and for women in Southern Europe. Scotland and Estonia had consistently low 5-year survival rates for all analyses compared with other countries.

Effect of age on survival

Survival clearly declined with age (Table 3). There was no clear pattern in the variation according to country, although there was less variation at younger ages. In a multivariate analysis (of proportional hazards), younger age at diagnosis favourably influenced survival ($P < 0.01$, Table 4).

Effect of histology on survival

Survival rates for the two major histological types of NPC, squamous cell and undifferentiated, were similar (Table 5). Generally, patients with squamous cell carcinoma had a lower survival than those with undifferentiated cancer in all ten countries included in the analysis. In a multivariate analysis (of proportional hazards), undifferentiated type (as well as the rare sarcoma type) favourably influenced survival ($P < 0.01$, Table 4).

Table 4. *Multivariate analysis of crude survival of patients with nasopharyngeal carcinoma in Europe,* 1978–1989 *(EUROCARE* II*)*

Variable	Hazard ratio	95% CI	*P* value
Age at diagnosis (years)			
15–44	1.00		
45–54	1.55	1.33–1.81	
55–64	2.04	1.77–2.35	
65–74	2.66	2.31–3.07	
75+	3.91	3.32–4.60	< 0.01
Histology			
Squamous	1.00		
Undifferentiated	0.82	0.74–0.90	
Sarcoma and other	0.80	0.69–0.92	< 0.01
Gender			
Male	1.00		
Female	0.93	0.84–1.01	ns
Period of diagnosis			
1978–1980	1.00		
1981–1083	0.98	0.86–1.13	
1984–1986	1.05	0.92–1.19	
1987–1989	1.02	0.90–1.17	ns

ns, non significant. CI, confidence interval.

Table 5. *Percentage crude survival of patients with nasopharyngeal carcinoma according to histology in* 10 *European countries,* 1978–1989† *(EUROCARE* II*)*

	1-year		5-year	
	Squamous % (SEM)	Undifferentiated % (SEM)	Squamous % (SEM)	Undifferentiated % (SEM)
Northern Europe				
Finland	70 (3.8)	80 (7.3)	40 (4.1)	39 (9.0)
Sweden*	63 (6.5)	79 (6.2)	28 (6.1)	58 (7.5)
Denmark	62 (3.6)	78 (3.5)	24 (3.3)	45 (4.4)
U.K.				
Scotland	59 (3.8)	56 (5.0)	21 (3.2)	23 (4.7)
England	62 (2.4)	60 (2.5)	29 (2.3)	30 (2.4)
Western and Central Europe				
France*	65 (7.0)	72 (11)	31 (7.7)	38 (13)
Southern Europe				
Spain*	55 (8.1)	88 (4.0)	26 (7.2)	39 (6.5)
Italy*	54 (5.3)	85 (3.1)	27 (4.7)	44 (4.3)
Eastern Europe				
Slovakia	65 (3.9)	76 (3.7)	33 (4.0)	40 (4.5)
Estonia	63 (7.8)	68 (7.0)	22 (7.0)	27 (7.4)
Europe‡	63 (1.3)	71 (1.3)	30 (1.2)	38 (1.5)
% Trimmed range§	55–65	60–85	22–33	27–45
% of Europe	15	38	40	50

* < 20% of the national population covered. †Only 15 countries participated between 1978–1989, of which only 10 had sufficient data for this analysis. ‡Unweighted figure. §After exclusion of extreme values. SEM, standard error of the mean.

Time trends in survival

There was no significant change in survival between 1978 and 1989 (Table 4).

DISCUSSION

The incidence of NPC in Europe is low, so this report from the EUROCARE study, covering one of the largest series of NPC, especially according to histological type, is particularly important. The study showed that generally there was little difference in survival between men and women with NPC, with a relative 5-year age-standardised survival rate of between 32 and 34%. Survival declined with age at diagnosis, confirming the results of previous reports [7, 14–16], but there was no change in prognosis between 1978 and 1989. In most countries, patients with squamous cell carcinoma, the more common form in Europe [17, 18], had a worse survival than those with undifferentiated carcinomas. With the exception of the U.K. (where survival for patients with either form of NPC was similar), survival of patients with undifferentiated cancer was 10–30% better than for squamous cell carcinoma. This is because undifferentiated tumours are generally less advanced and more sensitive to radiotherapy and chemotherapy, which are the standard treatments [19].

Variation in survival between countries was somewhat reduced after stratification according to histological type. As with other tumours, the relatively good survival rates in Scandinavia are likely to be due to centralised provision of adequate care, although the relatively small number of cases in some countries does not rule out the possibility of random variation. The poor survival rates in Scotland and Estonia, in particular, are probably due to the influence of alcohol-related comorbidity.

Stage is an important prognostic indicator [20], but unfortunately data on stage were not used in this study because they were only available in a few registries. Such data are often not reliably determined in population-based series especially if they include more elderly patients. Further studies are recommended investigating time trends and the role of stage and (centralised?) treatment, where data of a limited number of registries could be used.

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APPENDIX

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