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Original Paper

Survival of Adult Patients with Cancer of Soft Tissues or Bone in Europe

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Using data from the EUROCARE II database, relative survival rates for Europe were studied for adult patients with soft tissue sarcomas (STS) and bone cancers separately. Altogether 2,151 bone cancers and 5,845 STS were included. Survival analysis was carried out for each gender and the ratio between observed and expected survival calculated. One-year relative survival for bone cancer was 65% in men and 71% in women, and 5-year relative survival 45% in men and 51% in women. For STS 1-year relative survival was 78% for men and 79% for women and 5-year relative survival was 59% for both sexes. The variation in relative survival for bone cancer between countries was substantial, with the lowest rates seen in the Eastern countries. Denmark had the lowest rates of the Nordic countries, similar to those of Scotland. The variation in survival rates for STS was less pronounced, but still rates tended to be lower in Eastern European countries. The present analysis was carried out in the subset of European STS excluding visceral STS. To assess fully the international variation in survival a review of STS based on reported sarcoma morphology must be carried out. © **1998 Elsevier Science Ltd. All rights reserved.**

Key words: survival rates, soft tissue sarcoma, bone cancer, Europe
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INTRODUCTION

COMPARATIVE STUDIES between countries of population-based survival of cancer patients have proven essential for the evaluation of cancer care [1, 2], although imprecise with respect to details on treatment and stage. Such data indicate significant differences, raise questions and stimulate those responsible for cancer care to evaluate their performance in treatment and care, not only against results from centres of excellence but for healthcare systems as a whole.

One of the strengths of amalgamating data internationally is the ability to study even rare tumours—such as soft tissue sarcoma (STS) and bone cancer. The first EUROCARE project (30 registries, 800 000 patients) concentrated on major cancers and the comparability of data across countries with respect to registration and follow-up [1]. Although differences between countries are unlikely to be totally controlled, the consistent patterns for different sites, between different studies [3–9], and plausible explanations for the differences, give confidence in the findings.

STS and bone cancer are uncommon; each constituting less than 1% of all malignancies in most areas of the world [10–12]. They are a heterogeneous group of neoplasms, arising from the mesenchymal tissues and resemble the tissue of origin. STS, in particular rhabdomyosarcoma and fibrosarcoma [13], account for 4–8% of all childhood cancers, and almost 25% of all bone cancers occur in patients below the age of 20 years. Since this report focuses only on adult patients, a large proportion of bone cancers is not included, with the important exclusion of the young who have a somewhat poorer prognosis [4]. No major risk factor has been clearly identified for bone cancer and STS, although hereditary factors, certain environmental agents (radiation and chemicals) have been reported to be involved [10, 11, 14]. Other suspected factors include infectious and immunological mechanisms as indicated by the rise in Kaposi's sarcoma in AIDS patients [14]. Surgery is still the most effective curative treatment for sarcomas in bone and soft tissues and may often be curative if the cancer is localised [10, 11]. However, radiotherapy and combined radiotherapy and chemotherapy have proven effective for some specific types (e.g. liposarcomas, rhabdomyosarcomas) [10, 11].

*The EUROCARE Working Group for this study is listed in the Appendix.
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Comparability of data on STS and bone cancer is of major concern due to the differences in classification over time and how classifications are used in registries [14]. Often hampering comparability and analysis is how visceral STS is dealt with, and the confusion of bone metastasis and primary bone cancer. With rare cancers, such as STS and bone, misclassification may have a major impact on rates for incidence, mortality and survival. Consequently the expanded EUROCARE database from 17 countries and 45 cancer registries, with 3.5 million cancer patients, appeared suitable for the analysis of STS and cancer of the bone, allowing us to restrict the analysis to clearly defined cases. This report is the first report on survival for adults with a STS cancer across Europe, whereas sparse bone cancer data was presented in the first EUROCARE publication [1].

PATIENTS AND METHODS

STS and bone cancers were identified in the EUROCARE database using the ICD-O (International Classifications of Diseases for Oncology) [15]. Included were cases coded to the soft tissues (ICD-0; 171) and bone (ICD-O; 170) as primary cancers in patients more than 15 years of age. The distribution of specific morphological subtypes was examined.

Survival analysis was carried out on 7,996 adult STS and bone cancers diagnosed between 1985 and 1989 in 44 European population-based cancer registries. Some of these (Finland, Denmark, Scotland, Estonia, Slovenia, Iceland, Slovakia) cover the whole country, some a large proportion (England) and the rest up to 17% (Italy, Spain, France, The Netherlands, Germany, Sweden). Cases discovered at autopsy, patients first diagnosed with another tumour or known on the basis of a death certificate only (DCO) were excluded from survival analysis. The protocol specified a minimum follow-up of 5 years (unless death intervened).

Time trends were studied using data from the first EUROCARE project [1], including 20 registries in 13 countries. The data was subdivided into the following 3-year periods: 1978–1980, 1981–1983, 1984–1986 and 1987–1989. Gender-specific relative survival was computed as the ratio between the observed (crude) survival and the expected survival, derived from general mortality data [16].

RESULTS

2,151 adult patients with bone cancer and 5,845 patients with STS were identified, of which 91 and 78%, respectively, were histologically verified (Table 1). In bone, osteosarcomas constituted 28%, chondrosarcomas 24%, Ewing's sarcomas 12%, other specified 19% and unspecified or missing 17%. Fibro-, lipo- and leyomyosarcomas constituted 57% of all STS, whereas other specified, such as lymphosarcomas, haemangiosarcomas and others, totalled 20%, and unspecified and missing 23%. Excluding 140 STS and 133 bone cancer cases known only from death certificates and autopsies, the number of patients by age and proportion of men are presented in Tables 2 and 3.

The effect of gender and age on survival

The age-standardised relative survival for men and women after bone cancer (Table 4) or a STS (Table 5) was similar. Overall, 1-year relative survival for bone cancer was 65% in men and 71% in women and 5-year relative survival was 45% in men and 51% in women. For STS, the corresponding figures were approximately 10% higher (Table 5).

Table 1. *Total number (*n*) and per cent (%) histologically verified soft tissue sarcomas and bone cancers by country,* 1985–1989 *(EUROCARE* II*)*

	Soft tissue sarcoma		Bone cancer	
Country	*n*	% HV	*n*	% HV
Northern Europe				
Iceland	19	100	10	100
Finland	511	98	140	96
Sweden*	203	100	51	100
Denmark	510	99	289	61
U.K.				
Scotland	450	95	146	86
England	2276	82	772	79
Western and Central Europe				
The Netherlands*	76	100	25	96
Germany*	131	94	43	86
Austria*	43	88	12	67
Switzerland*	43	100	11	100
France*	121	99	40	98
Southern Europe				
Spain*	227	97	93	83
Italy*	430	92	192	73
Eastern Europe				
Slovenia	120	98	53	91
Slovakia	431	96	169	71
Poland*	99	89	54	56
Estonia	155	97	51	77
Europe	5845	91	2151	78

* < 20% of the national population covered. HV, histologically verified.

There was little difference in survival for the various age-classes (data not shown) [15], apart from a somewhat poorer relative survival among the older patients, being almost halved in those aged 75 years or more with bone cancer, but only approximately 10% less in STS patients.

Inter-country differences in survival

The variation in relative survival for bone cancer between countries was substantial with the lowest 5-year rates (20–40%) seen in the Eastern European countries. The highest 5-year rates (61–70%) were seen in Sweden and France (Table 4). Denmark had the lowest rates of the Nordic countries, similar to those from Scotland. Much less variation was seen for STS, where 5-year survival rates were similar, taking into consideration the wide confidence intervals (CIs), although again Eastern countries tended to have lower rates.

Time trends in survival

Between 1978 and 1989, 1-, 3- and 5-year relative survival improved in Europe as a whole (Figure 1). The improvement was most marked for bone cancer (Figure 1a), with one year relative survival increased from 62 to 77%, and 5-year survival from 40 to 53%. For STS, 1-year relative survival improved from 71 to 81% and 5-year relative survival improved from 55 to 59%.

DISCUSSION

Despite probable differences in the definition of STS [14] and the probable inclusion of some metastasis, in particular

Table 2. Number of bone cancer cases† by age and country, proportion of men and patients 65 years of age or more, 1985–1989 (EUROCARE II)

	Age at diagnosis (years)							
	15–44	45–64	55–64	65–74	75+	Total	% Men	% < 65 years
Northern Europe								
Iceland	4	2	1	2	1	10	70	30
Finland	54	17	30	25	14	140	51	27
Sweden*	14	5	6	15	11	51	71	51
Denmark	54	28	40	65	102	289	53	50
U.K.								
Scotland	51	7	28	30	27	143	50	40
England	234	70	129	147	148	728	55	41
Western and Central Europe								
The Netherlands*	8	3	6	3	5	25	48	32
Germany*	17	6	4	8	3	38	63	29
Austria*	2	1	3	1	1	8	63	25
Switzerland*	5	1	1	1	3	11	55	36
France*	22	3	9	3	3	40	60	15
Southern Europe								
Spain*	30	13	14	12	8	77	42	26
Italy*	45	22	40	46	29	182	56	41
Eastern Europe								
Slovenia	22	9	6	5	5	47	57	21
Slovakia	51	22	29	21	13	136	56	25
Poland*	20	6	6	9	6	47	62	32
Estonia	13	11	10	7	5	46	52	28
Europe	646	226	362	400	384	2018	57	39

* < 20% of the national population covered. †Excluding 121 cases known from death certificate only (DCO) and 12 known only from autopsy.

Table 3. Number of patients with soft tissue sarcoma† by age and country, proportion of men and patients 65 years of age or more, 1985–1989 (EUROCARE II)

	Age at diagnosis (years)							
	15–44	45–54	55–64	65–74	75+	Total	% Men	% < 65 years
Northern Europe								
Iceland	8	6	0	1	4	19	63	26
Finland	133	60	99	102	110	504	50	42
Sweden*	38	19	28	57	57	199	54	57
Denmark	178	60	79	104	89	510	55	38
U.K.								
Scotland	108	54	86	95	99	442	50	44
England	542	259	398	497	517	2213	52	46
Western and Central Europe								
The Netherlands*	21	13	18	11	13	76	59	32
Germany*	33	25	27	18	20	123	56	31
Austria*	9	4	8	8	10	39	44	46
Switzerland*	19	5	2	8	9	43	58	40
France*	36	17	21	23	24	121	55	39
Southern Europe								
Spain*	63	26	42	42	50	223	52	41
Italy*	86	67	99	81	90	423	55	40
Eastern Europe								
Slovenia	41	14	24	19	21	119	61	18
Slovakia	112	66	92	78	58	406	51	33
Poland*	29	16	23	12	16	96	51	29
Estonia	30	21	43	30	25	149	43	37
Europe	1486	732	1089	1186	1212	5705	53	42

* < 20% of the national population covered. †Excluding 111 cases known from death certificate only (DCO) and 29 known only from autopsy.

in countries with lower histological confirmation, our data have shown some but not major survival differences between different areas of Europe. The small differences seen, such as in the Nordic countries with a lower bone cancer survival in Denmark, can in part be explained by the age-distribution of cases and the low proportion of histological verified cases which undoubtedly means a high inclusion of metastasis as true bone cancers. In contrast, the Danish STS patients seemed to be younger than in the other Nordic countries, hence the opposite effect is seen on survival. Survival in

Table 4. *Age-standardised relative* 1- *and* 5-*year survival (%) following bone cancer, by country† and gender,* 1985–1989 *(EUROCARE* II*)*

	Men		Women	
	1 year % (95% CI)	5 year % (95% CI)	1 year % (95% CI)	5 year % (95% CI)
Northern Europe				
Finland	75 (65–87)	55 (42–71)	81 (72–91)	54 (43–67)
Sweden*	83 (75–93)	61 (46–80)	76 (63–91)	70 (57–87)
Denmark	56 (49–64)	37 (29–46)	67 (60–75)	49 (41–58)
U.K.				
Scotland	67 (56–80)	32 (24–43)	67 (58–78)	47 (37–60)
England	66 (62–71)	48 (43–54)	75 (71–79)	54 (49–60)
Western and Central Europe				
France*	74 (66–82)	69 (60–80)	76 (58–99)	63 (43–93)
Southern Europe				
Spain*	69 (53–89)	43 (27–68)	84 (73–98)	66 (51–86)
Italy*	65 (57–76)	37 (28–49)	75 (66–86)	57 (46–70)
Eastern Europe				
Slovenia	59 (43–81)	20 (13–32)	53 (36–77)	29 (16–51)
Slovakia	41 (34–51)	27 (19–37)	50 (39–64)	40 (28–57)
Estonia	39 (23–67)	34 (16–71)	71 (57–89)	26 (15–46)
Europe	65 (60–70)	45 (39–52)	71 (66–77)	51 (45–58)

* < 20% of the national population covered. †Data from countries with less than 50 cases were only included in the overall 'Europe' category. CI, confidence interval.

Table 5. *Age-standardised relative* 1- *and* 5-*year survival (%) following soft tissue sarcoma, by country† and gender,* 1985–1989 *(EUROCARE* II*)*

	Men		Women	
	1 year % (95% CI)	5 year % (95% CI)	1 year % (95% CI)	5 year % (95% CI)
Northern Europe				
Finland	75 (70–81)	51 (44–59)	74 (69–80)	48 (42–56)
Sweden*	84 (76–92)	65 (55–77)	82 (74–91)	66 (55–78)
Denmark	81 (76–87)	62 (55–70)	87 (82–92)	70 (63–78)
U.K.				
Scotland	71 (66–78)	50 (43–59)	74 (68–80)	50 (43–59)
England	74 (71–77)	55 (52–59)	73 (70–76)	54 (51–58)
Western and Central Europe				
The Netherlands*	73 (60–88)	50 (29–85)	85 (70–10)2	51 (35–75)
Germany*	87 (79–96)	70 (52–94)	85 (75–95)	74 (61–90)
France*	73 (62–87)	58 (42–80)	86 (77–96)	58 (43–77)
Southern Europe				
Spain*	75 (68–84)	69 (59–81)	75 (67–84)	53 (43–65)
Italy*	80 (74–85)	59 (52–67)	77 (71–84)	57 (49–65)
Eastern Europe				
Slovenia	79 (68–91)	54 (40–72)	74 (63–87)	46 (33–64)
Slovakia	67 (60–75)	39 (29–52)	71 (65–78)	54 (46–63)
Poland*	68 (54–86)	35 (20–60)	73 (62–86)	43 (31–59)
Estonia	60 (48–76)	36 (25–50)	72 (63–82)	47 (35–62)
Europe	78 (75–81)	59 (53–65)	79 (76–82)	59 (55–63)

* < 20% of the national population covered. †Data from countries with less than 50 cases were only included in the overall 'Europe' category. CI, confidence interval.

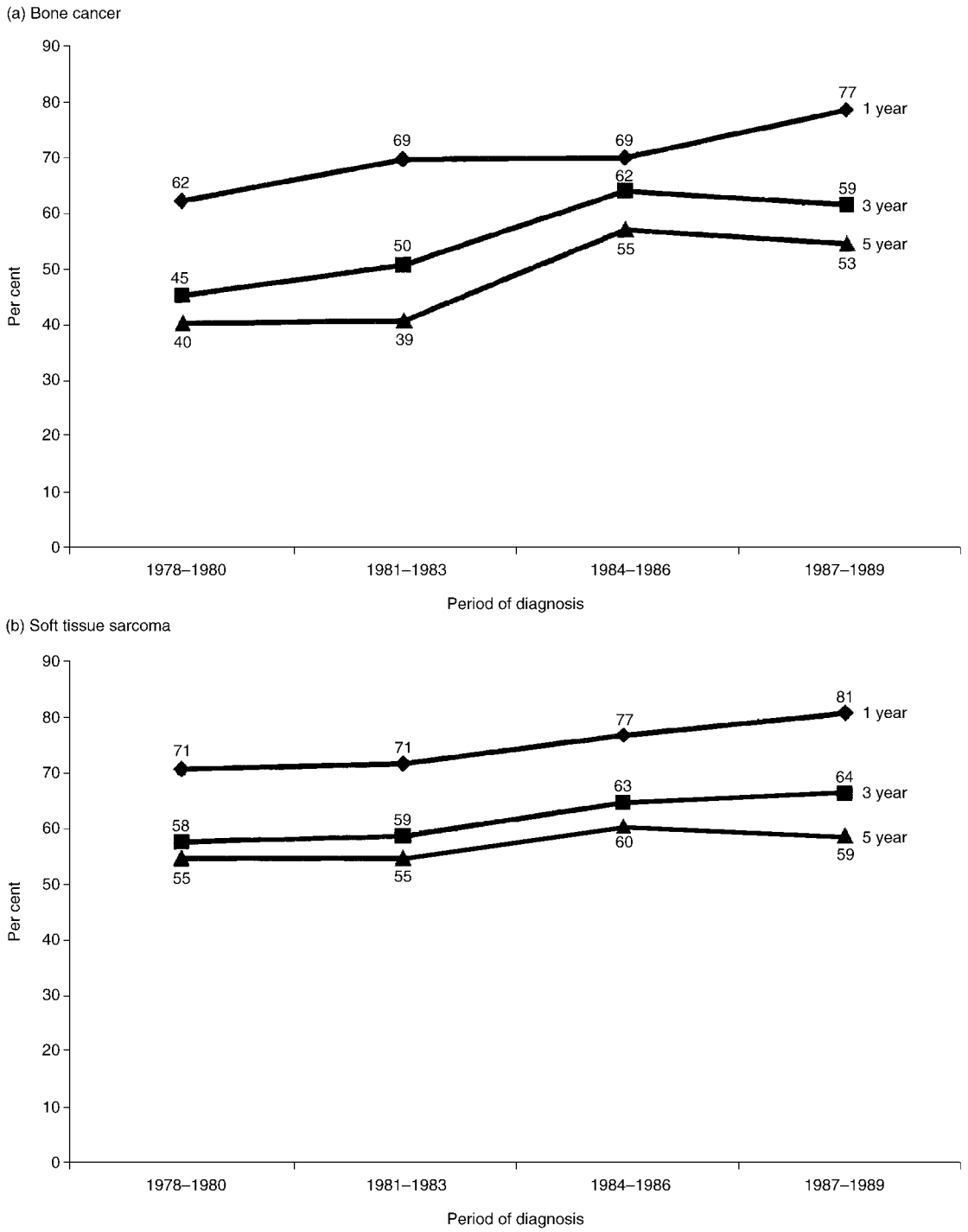

Figure 1. Trend in relative survival for patients with (a) bone cancer and (b) soft tissue sarcomas in Europe, 1978–1989 (EUROCARE II). Based on 20 registries from 13 countries which contributed data for the whole period 1978–1989.

Eastern Europe is in line with what was seen in the first EUROCARE analysis [1].

Survival improved since 1978, both for bone cancer and for STS. This may be somewhat surprising, inasmuch as surgery dominates treatment and neither new radiotherapy regimes nor drugs have been widely approved in the recent period under study. One important factor may be development of special centres for the diseases, which may lead to lower rates of local recurrences as demonstrated in Sweden [17]. However, even if improvements in therapy on Ewing's and osteosarcoma have taken place and some clinical series have reported better survival for STS [17, 18], one could speculate that diagnostics in general have improved in this period, leading to better survival. One other possibility includes increased use of chemotherapy in older aged patients. Unfortunately, our data did not allow analysis by stage or treatment of disease and it is thus impossible to say if any of the change may be related to these factors.

Estimation of survival is complicated by the wide variety of morphological subtypes and sites for both STS and bone cancer. Only a few studies have estimated survival by histological groups, which is an important predictor. However, this was done in a Dutch study [9], where 5-year survival rates pretty close to those published from the SEER data were found [7, 11]. Dermatofibrosarcoma, due its superficial nature, has a good prognosis with a 5-year survival rate over 90%, followed by liposarcoma (73%). The US and Dutch data differ with respect to fibrosarcoma (US 71%, Dutch 55%), rhabdomyosarcoma (US 52%, Dutch < 10%), leiomyosarcoma (US 29%, Dutch 40%) and angiosarcoma (US 33%, Dutch 20%). In bone, best 5-year relative survival rates have been found for chondrosarcoma (68%), followed by osteosarcoma (45%) and Ewing's sarcoma (40%) based on data from SEER [10]. Although our data could be analysed by morphological subtypes, we have not yet done so because this would require a pathologist review with re-typing and classification of the relatively large proportion (17–23%) of cases unspecified or undetermined. Also, other data unavailable to us, such as malignancy grade and tumour size, should be included [19].

The present analysis provides an important baseline for survival after bone cancer or STS in Europe, excluding visceral STS which are included in the organ-site where they appear, such as the corpus uteri, stomach, skin, lung, etc. Irrespective of the registration coding, classification problems and the possible influence on rates by misclassified metastasis, the survival rates are reasonably stable across borders and do show some North–South, West–East trends, where a plausible explanation could be social differences and differences in healthcare. Even if these relatively rare cancers cannot be rated as a major public health problem, it is obvious, based on this large dataset, that improvements in survival may be possible in a number of countries. Future analysis should include variables such as stage, morphological type and standard treatment in order to facilitate the explanation for observed differences in survival.

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APPENDIX

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