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Childhood Malignancies in Germany—Methods and Results of a Nationwide Registry

P. Kaatsch, G. Haaf and J. Michaelis

Since 1980, a nationwide registry of childhood malignancies has been established in the Federal Republic of Germany. The registry combines features of a population-based and a hospital-based registry. Basic registry data are complemented and validated by data from all ongoing clinical trials in paediatric oncology. Descriptive analyses are presented for the first 13 years of operation of the registry. In addition, time trends and regional variations of incidence within the Federal Republic of Germany are shown. A brief description of completed and ongoing registry-based epidemiological studies is given.

Key words: childhood malignancies, cancer registry, epidemiological studies, clinical trials, cancer incidence, secondary malignancies

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INTRODUCTION

In 1980, a nationwide registry of childhood malignancies was initiated by the German scientific society for paediatric oncology and haematology. The registry is maintained at the Institut für Medizinische Statistik und Dokumentation (IMSD) at the University of Mainz, Germany. From 1980 to 1990, all incident cases of childhood malignancies in the former Federal Republic of Germany were reported to the registry. Since 1991, cases from the area of the former German Democratic Republic have also been included. The registry is a combination of a population-based and hospital-based registry.

This paper describes the methodology of the registry and gives some results from the first 13 years of operation. The standard presentation of incidence, relative frequencies, survival rates, etc. of the most common malignancies may serve as a reference for descriptive epidemiology of childhood cancer in the F.R.G. The German data are compared with observations from other registries in order to illustrate international differences and similarities. In addition, time trends and regional variations within Germany are presented. Finally, a short description of completed and ongoing registry-based epidemiological studies is given.

MATERIALS AND METHODS

General principles of the registry

The German registry combines features of a population-based and a hospital-based registry and is intended to include all children diagnosed below age 15 years with malignant disease or any form of CNS tumour. More than 70% of these children are entered into clinical trials, which thus form a major source of data. Therefore, an integrated documentation sequence and information flow between the cancer registry, treating hospitals and trial study centres have been established.

More than 130 paediatric hospitals and centres for paediatric oncology report all their cancer patients on a voluntary basis to the registry. Because of the German legislation on data privacy and security, informed consent of the patients or their parents is necessary for the storage of personal data in the registry. As only 0.6% of the families refuse this consent, loss of data due to this condition is negligible.

For the classification of diseases, we use a scheme suggested by Birch and Marsden [1]. This is specifically adapted to childhood malignancies and better differentiated than the International Classification of Diseases.

The age-adjusted incidences presented in this paper are calculated in the same way as performed by Parkin and associates [2], i.e. the world standard population for children below 15 years of age is used. The cumulative rate is the sum of the age-specific incidences for each year of age. This is an approximation to the cumulative risk, which is the risk of an individual developing a malignancy during the first 15 years of life [3]. Follow-up data exist for more than 80% of all registered malignancies. Estimations of 3- and 5-year survival rates (Kaplan–Meier) are given.

Documentation and flow of information

After admission of a newly diseased individual to one of the co-operating hospitals, a notification form is sent to the Institut für Medizinische Statistik und Dokumentation (IMSD). This contains patient identification data, a tentative diagnosis and information on whether this patient will be included in one of the ongoing clinical trials. In response to the initial report form, the IMSD send a set of tumour-specific basic documentation forms to the co-operating clinician. For patients included in clinical trials, the basic documentation forms will be returned directly to the relevant trial centre. There, the documented data are first checked with respect to completeness, medical

Correspondence to P. Kaatsch.
The authors are at the Institut für Medizinische Statistik und Dokumentation der Johannes Gutenberg-Universität Mainz, Langenbeckstraße 1, D-55101 Mainz, Germany.
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plausibility and consistency and only then are they sent to the IMSD. Because the trial centres are in close contact with the treating physicians, the data quality in the registry is very high. For the long-term follow-up organised by the IMSD, the patient's current status is requested simply by using printouts for all patients, for whom no information has been sent to the IMSD during the past 12 months. More details have been described elsewhere [4].

RESULTS

All presented results are related to the F.R.G. before the unification with the former G.D.R., although for 1991 and 1992, first calculations of incidence for the total F.R.G. were made by the registry. To date, the incidence for the eastern region of Germany is approximately 85% of the incidence estimated for the western region, but is very close to the rates published from the former cancer registry of the GDR. During the first 5 years from 1980 to 1984, the registry covered approximately 80% of the estimated incidence in the F.R.G. Thereafter, completeness has increased to an estimated 95%.

Incidence rates, sex ratios, survival rates and secondary malignancies

Table 1 shows summary figures for all childhood malignancies and the major subgroups.

In the period 1980–1992, a total of 16471 children below 15 years of age were registered. Calculations of incidence rates are based on the time period of 1987–1992. For all malignancies, the crude incidence is 14.1/100000 children below 15 years of age per year. It is higher for boys (15.3/100000) than for girls (12.7/100000). The incidence in the first 5 years of life is nearly twice as high as in the age group 5 to 14 years. Due to the fact that, in Germany, there are relatively fewer children in this younger age group than in the world standard population (34.1 versus 38.7%), the adjusted incidence (14.4/100000 per annum) is somewhat higher than the crude rate. The cumulative rate is 208.6/100000. The median age at diagnosis is 6 years 1 month and the overall 5-year survival rate is 70%.

Comprising 34.5% of all registered malignancies, leukaemias constitute the most common disease group. Acute lymphocytic leukaemia with an incidence of 3.7/100000 is the most common single malignant disease. Its maximum incidence rates occur at the ages of 2 and 3 years (8.5/100000) and the median age is 4 years 10 months. The 5-year survival rate is 77%. Acute non-lymphocytic leukaemia has an incidence of 0.7/100000 and a rather poor overall prognosis with a 5-year survival rate of 46%. Other leukaemias in childhood are the chronic myeloid leukaemias with a relative frequency of 0.8%.

Lymphomas constitute 11.2% of all malignancies. Amongst this, non-Hodgkin's lymphoma with 0.8 and Hodgkin's disease with 0.6/100000 are the most common diseases. Both are pronouncedly more frequent in boys than girls, with sex ratios of 2.6 and 1.5 boys to 1 girl, respectively. Besides the bone tumours, Hodgkin's disease has the highest median of age of childhood malignancies. Hodgkin's disease shows (besides retinoblastoma) the best cure rate of childhood malignancies with a 5-year survival rate of 95%.

Birch and Marsden [1] have proposed to include Langerhans cell histiocytosis in the group of reticuloendothelial neoplasms, although this disease is not a neoplasm in a narrow sense. They conceded that this is a matter of controversy, but we use their suggested classification in total, as Parkin and associates did [2]. Our registry—apart from the Manchester Children's Tumour Registry in the U.K.—is the only one which registers this disease systematically [5]. Langerhans cell histiocytosis occurs in 3.0% of all registered cases and has a good prognosis with an 88% 5-year survival rate. Particularly in the first year of life, the preponderance of boys is pronounced.

Both benign and malignant CNS tumours are registered. For this group of diseases, the incidence of 2.5/100000 is underestimated because not all of these tumours are treated with chemotherapy, and therefore some are not seen by paediatric oncologists who are the main source of registrations. However, since improved co-operation started between the different disciplines involved in the treatment of this specific disease group, reporting has improved.

Tumours of the sympathetic nervous system occur with a relative frequency of 7.7%. Neuroblastoma with a relative frequency of 7.2% and an incidence of 1.1/100000 is the most frequent single disease among all solid tumours. It is the most common malignancy in the first year of life [6] with an age-specific incidence of 6.2/100000. Prognosis in the tumour depends very strongly on stage at diagnosis. Whereas stage I frequently disappears spontaneously, stage IV has a very poor prognosis (except stage IVS which mainly occurs at the first year of life with a prognosis like stage II or stage III patients). The overall 5-year survival rate is 55%.

Retinoblastoma has an incidence of 0.4/100000 and the age-specific incidence for children in the first year of life is 2.3/100000. This disease has the lowest median of age of all childhood malignancies (1 year 3 months). One paediatric hospital in particular in Germany is mainly involved in treating retinoblastomas. From this hospital, the comprehensive reports of newly diseased children—most of them with bilateral tumours—are received. The unilateral retinoblastomas were often treated in non-paediatric hospitals which generally do not contribute to our registry. We do not know how complete our registry for these unilateral tumours is.

Within the group of kidney tumours, nephroblastoma has an incidence of 0.9/100000. The tumour is the second most frequent of all solid tumours and occurs mainly in the first 5 years of life. The overall prognosis with 86% 5-year survival rate is good.

Hepatic tumours account for 1.1% of all malignancies and include hepatoblastoma with 0.8% and carcinoma with 0.2%.

Osteosarcoma and Ewing's sarcoma are the most frequent tumours of bone (2.8 and 1.8%, respectively). They have the highest median age of all childhood malignancies and occur frequently beyond the 15th year of life.

Of the soft tissue sarcomas, the rhabdomyosarcoma is the most frequent with an incidence of 0.6/100000. Embryonal rhabdomyosarcomas are more common than alveolar.

The group of germ cell tumours is very heterogeneous and contains both gonadal and non-gonadal malignancies. It might be possible that some benign teratomas reported as "unspecified" were included here. The incidence in the first year of life is 3.2/100000, making this one of the most frequent malignancies in this age group. In girls, a second peak is observed after 8 years of age. The germ cell tumours belong to one of the very few groups of childhood malignancies that is more common in girls than in boys (1:0.7).

Carcinoma and other epithelial neoplasms occur very rarely in childhood. They show a relative frequency of 0.8% [excluding carcinoma of kidney (0.1%) and liver (0.2%), which are included in other disease groups].

329 patients with secondary malignancies were registered. Approximately half of these cases were primarily diagnosed after

Table 1. Frequencies, incidence rates and other descriptive statistics of malignancies in childhood (as classified by Birch and Marsden [1]; children below 15 years of age; diagnosed between 1980 and 1992; incidence rates and sex ratio based on data from 1987 to 1992)

Diagnosis	Frequency		Incidence per 100 000 per annum										Survival rate (%)	
					Age group (years)									
	Relative (%)	Absolute	Male	Female	0	1–4	5–9	10–14	Crude	Adjusted	Cumulative	Sex ratio (male:female)	3 years	5 years
Total	100	16 471	15.3	12.7	24.9	19.6	11.1	10.0	14.1	14.4	208.6	1.2:1	75	70
Leukaemias	34.5	5 682	5.1	4.1	3.6	8.0	3.9	2.7	4.7	4.8	68.8	1.2:1	76	71
Acute lymphocytic	27.8	4 584	4.1	3.3	1.8	6.9	3.3	1.8	3.7	3.9	55.1	1.2:1	83	77
Acute non-lymphocytic	4.8	793	0.8	0.6	1.4	0.8	0.5	0.7	0.7	0.7	10.5	1.3:1	49	46
Lymphomas	11.2	1 862	2.1	1.0	0.1	0.9	1.8	2.2	1.5	1.5	23.2	2.1:1	88	86
Hodgkin's disease	4.6	762	0.7	0.5	0.0	0.2	0.5	1.1	0.6	0.5	8.6	1.5:1	97	95
Non-Hodgkin's lymphoma	5.6	926	1.1	0.4	0.1	0.6	0.9	1.0	0.8	0.8	11.7	2.6:1	79	77
Reticuloendothelial neoplasms	3.4	550	0.5	0.4	1.4	0.6	0.3	0.2	0.5	0.4	6.7	1.3:1	82	81
Langerhans cell histiocytosis	3.0	488	0.5	0.4	1.2	0.6	0.3	0.2	0.4	0.4	6.3	1.4:1	90	88
CNS tumours	16.3	2 692	2.7	2.3	2.6	3.1	2.7	1.8	2.5	2.6	38.0	1.2:1	61	55
Astrocytoma	5.1	832	0.9	0.8	0.7	1.0	1.0	0.6	0.9	0.9	12.8	1.0:1	69	67
Medulloblastoma	3.8	633	0.7	0.4	0.3	0.7	0.7	0.3	0.5	0.6	8.1	2.0:1	57	50
Sympathetic nervous system	7.7	1 266	1.2	1.1	6.2	1.9	0.3	0.1	1.1	1.2	16.0	1.1:1	60	56
Neuroblastoma	7.2	1 191	1.1	1.0	6.2	1.8	0.3	0.1	1.1	1.2	14.9	1.1:1	59	55
Retinoblastoma	2.5	414	0.4	0.4	2.3	0.8	0.1	<0.1	0.4	0.6	5.7	1.1:1	96	96
Kidney tumours	6.4	1 061	0.9	0.9	2.6	2.0	0.5	0.1	0.9	1.0	13.4	1.0:1	87	86
Nephroblastoma	6.1	1 006	0.9	0.8	1.9	2.0	0.5	0.1	0.9	1.0	12.4	1.0:1	87	86
Hepatic tumours	1.1	174	0.2	0.1	0.8	0.3	<0.1	<0.1	0.2	0.2	2.3	1.5:1	52	47
Bone tumours	5.1	843	0.6	0.6	0.1	0.2	0.5	1.2	0.6	0.6	9.5	1.0:1	69	61
Osteosarcoma	2.8	464	0.3	0.3	<0.1	<0.1	0.3	0.7	0.3	0.3	4.8	0.9:1	71	64
Ewing's sarcoma	1.8	296	0.3	0.2	0.0	0.1	0.2	0.4	0.2	0.2	3.4	1.3:1	68	58
Soft tissue tumours	6.9	1 129	1.0	0.9	1.7	1.2	0.6	0.8	0.9	0.9	13.8	1.1:1	71	66
Rhabdomyosarcoma	3.9	646	0.6	0.5	0.6	0.9	0.4	0.4	0.6	0.6	8.2	1.0:1	71	63
Germ cell tumours	3.7	617	0.5	0.7	3.2	0.5	0.3	0.5	0.6	0.6	9.0	0.7:1	85	83
Carcinoma and epithelial tumours	0.8	139	0.1	0.1	<0.1	0.1	0.1	0.2	0.1	0.1	1.9	0.8:1	73	68
Others	0.3	42	<0.1	0.1	0.1	<0.1	<0.1	0.1	<0.1	<0.1	0.5	0.6:1	No valid data	No valid data

the registry began and were notified by routine follow-up. The other cases were obtained from spontaneous collection of secondary malignancies, which has been made available to our registry [7]. For these patients, Table 2 shows both the most common primary and most common secondary malignancies. The frequency of these primary malignancies mostly corresponds to the frequencies of the incident cases observed in the registry as a whole (see Table 1). Only retinoblastoma as a primary malignancy is remarkably more frequent than in the population of the registry (8.8% compared to 2.5%). Most common secondary malignancies were CNS tumours, acute non-lymphocytic leukaemia, osteosarcoma and thyroid carcinoma. Compared with the distribution of all childhood malignancies, remarkable deviations were observed for thyroid carcinoma. As a primary malignancy in childhood, it appears in less than 1%, but amounted to 6.1% of all secondary malignancies.

International comparison, time trends, regional variability of incidence rates

For evaluating the completeness of the German registry and geographical variations, one can compare the data with that from other registries. Parkin and co-workers have published a monograph on childhood cancer incidence [2] which provides an excellent basis for such comparisons. From this publication, we have selected 24 registries that have at least 100 registrations per year and which each contributed in total 999 cases or more to the monograph. For the most common diseases, Table 3 shows the lowest and highest incidence as well as the median incidence observed in the selected registries. These are compared with the incidence rates in Germany for the years from 1987 to 1992. Nearly all incidence rates for the German registry are higher than the corresponding median. While for the most frequent single diseases, the incidence is markedly higher than the median, the incidence for CNS tumours is only slightly higher than the observed median incidence. This indicates an under-reporting of the CNS tumours.

One of the goals of epidemiological cancer registries is to analyse possible time trends of incidences. Figure 1 shows the age-adjusted incidences by calendar years using a uniform age distribution with equal numbers in each 1-year age group for all malignancies, leukaemias and CNS tumours. The incidence of leukaemia is impressively constant over the whole period especially since 1985, with a range between 4.4 and 4.6/100 000. This is an indication of uniform registration. Only in 1992 was a higher incidence observed. In contrast, the curve for CNS tumours shows an increasing trend from the beginning of registration up to 1987. This is due to the aforementioned intensified co-operation between all clinicians involved in treating this special group of tumours. One can state that for all malignancies in total the increased incidence in the first 7 years is attributable to a more complete registration, especially in CNS tumours. From 1987 onwards, the completeness has reached a nearly stable level. The annual incidence rates vary from 13.5 to 14.6 new cases per 100 000.

Regional variability of incidence rates is routinely analysed on three levels (16 Bundesländer, 328 Landkreise and 8500 municipalities) and corresponding maps are produced annually. Table 4 shows disease-specific incidence rates according to urban–rural status of the corresponding Landkreise based on a classification of an official German agency [8]. In general, the incidence rates in rural regions are lower than in urban ones. This can be observed in nearly every disease group. For all malignancies, a factor of 1.2 between largest towns and rural regions is observed. The mentioned underascertainment in the first years of registration was more pronounced in the rural than in the urban regions. However, this fact only slightly influences the magnitude of the described difference. It does not explain the observed variation on principle. Lymphomas and tumours of kidney and bone have their highest incidence rates in the most urban regions and their lowest rates in the most rural ones. CNS tumours have their lowest incidence in the pure rural regions but their second lowest incidence in the largest towns, so that in this disease group, a trend as seen for all the other diseases could not be observed. In contrast to our data in leukaemia, Alexander and associates [9] found a higher incidence in rural than in urban regions, but these results achieved no significance levels, and are based only on a small number of patients.

EPIDEMIOLOGICAL STUDIES

Based on the existing structures of co-operation, we are able to conduct epidemiological studies. Some of these will be briefly described in order to give an indication of how the registry can operate in this field.

One ecological study relates to the incidence of childhood malignancies in the vicinity of major German nuclear installations [10]. The main result is that the relative risks for all malignancies and for acute leukaemia within a 15-km radius of the installations were not increased. Additional explorative analyses, among others, show increased relative risks for acute leukaemia in children below 5 years of age, and especially in the 5-km circles of the oldest plants. An increased incidence was also found in regions where nuclear power plants have been planned. In a subsequent ongoing case–control study, we want to analyse questions generated from this ecological study.

For 1988, we observed a marked increase in the incidence of neuroblastoma in children below 1 year of age. The excess cases were almost exclusively observed in areas with increased fall-out from the Chernobyl accident. A subsequent case–control study

Table 2. 329 patients with secondary malignancies

Most common primary malignancies	Frequency		Most common secondary malignancies	Frequency	
	Absolute	Relative (%)		Absolute	Relative (%)
Acute lymphocytic leukaemia	94	28.6	CNS tumours	66	20.1
CNS tumours	40	12.2	Acute non-lymphocytic leukaemia	43	13.1
Retinoblastoma	29	8.8	Osteosarcoma	36	10.9
Hodgkin's disease	26	7.9	Thyroid carcinoma	20	6.1
Non-Hodgkin's lymphoma	20	6.1	Non-Hodgkin's lymphoma	16	4.9
Rhabdomyosarcoma	17	5.2	Acute lymphocytic leukaemia	14	4.3

Table 3. Incidence rates from the German registry (based on data from 1987 to 1992) in comparison to other large registries

Diagnosis	Incidence rates per 100 000 per annum			
		Foreign registries		
	German registry	Minimum	Median	Maximum
Acute lymphocytic leukaemia	3.9	1.1	2.9	3.9
Acute non-lymphocytic leukaemia	0.7	0.3	0.6	1.0
Hodgkin's disease	0.5	0.1	0.4	0.9
Non-Hodgkin's lymphoma	0.8	0.0	0.6	1.8
CNS tumours	2.6	0.8	2.5	3.4
Neuroblastoma	1.2	0.3	0.9	1.3
Nephroblastoma	1.0	0.4	0.7	1.0
Osteosarcoma	0.3	0.2	0.3	0.4
Ewing's sarcoma	0.2	0.0	0.2	0.3
Rhabdomyosarcoma	0.6	0.1	0.4	0.6
Germ cell tumours	0.6	0.1	0.4	0.6
All malignancies	14.4	7.1	12.9	14.7

Incidence rates age-adjusted to the World Standard Population.

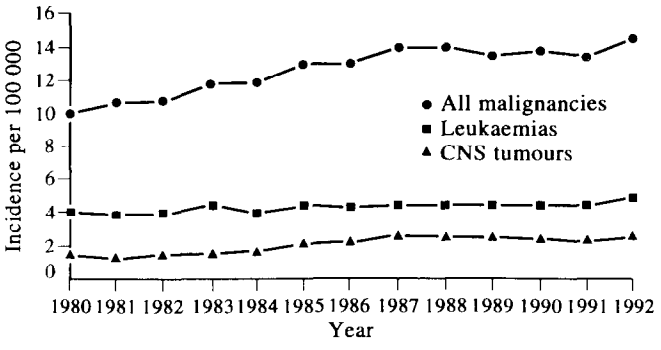

Figure 1. Incidence rate (per 100 000 children below 15 years of age per annum; age adjusted to a uniform age distribution) for all malignancies, leukaemias and CNS tumours by calendar years.

did not give any additional hints about increased radioactive exposure of the children and their parents. However, an observed change in the distribution of disease stages indicated that intensified diagnostic procedures may have led to the observed peak of incidence. This might be explained by increased anxiety of doctors living in regions with higher contamination by the accident. Formal screening projects had not been established at this time. In order to study possible effects from the Chernobyl accident, we are taking part in the European Childhood Leukaemia/Lymphoma Incidence Study (ECLIS), which is co-ordinated by IARC in Lyon, France [11].

Another case–control study is being run in close co-operation with the German Cancer Research Centre in Heidelberg in order to explore whether there is an association between the incidence of leukaemias and parvovirus infections. The recruitment phase of this virological–epidemiological study has terminated and the data are currently being analysed.

Additional studies are currently being performed. Among others, they are related to possible effects of electromagnetic fields, and they serve to validate the hypothesis that vitamin K prophylaxis against haemorrhagic disease of newborns could lead to an increased risk of leukaemia.

In the aforementioned studies (except ECLIS), information is collected by means of a questionnaire completed by parents of both patients and controls concerning possible aetiological factors. The comprehensive experiences of the Children's Cancer Group could be taken into consideration for developing this questionnaire [12]. We have observed that the parents are very co-operative in such inquiries. In current studies, we additionally perform telephone interviews. Because of the encouraging response, we use a reduced questionnaire routinely for each newly diseased child. This is used in order to collect some epidemiological data systematically. In addition, we obtain parents' consent for collecting further information when conducting future investigations.

DISCUSSION

The paper describes the methodological approach and operation during the first 13 years of the German registry of childhood malignancies. In the western part of Germany, approximately 1400 newly diseased cases were reported every year. We estimate that approximately 95% of the total incidence is covered. Only for the CNS tumours is there still a systematic under-reporting. The registry is operated on a voluntary basis with the co-operation of the treating clinicians.

More than 70% of all German children with malignant diseases are treated within controlled clinical trials. An integrated documentation system has been developed to serve the purposes both of the clinical trials and of the registry. This facilitates the documentational work of the treating physicians and enhances the quality of the data stored in the registry. Motivating factors for the co-operation are participation in these clinical trials and individual feedback of information to the co-operating hospitals (annual reports, statistical summaries, specific analyses on demand).

The treatment of childhood malignancies has improved dramatically during the last 20 years. Therefore, long-term follow-up of the survivors is now of more concern. As long as the patients stay in contact with their treating physicians, it is relatively easy to obtain follow-up information. After the patients are no longer regularly seen by the paediatric oncologists, we try

Table 4. Incidence rates (per 100 000 children below 15 years of age per annum) in urban and rural regions by disease groups (based on data from 1980 to 1992)

	Population density >300 inhabitants per square kilometre			Population density 150–300 inhabitants per square kilometre		Population density <150 inhabitants per square kilometre
		Surroundings				
		Population density				
Disease groups	Towns	Higher	Lower	Towns	Surrounding regions	Rural
Leukaemias	4.4	4.5	4.5	4.4	4.4	4.1
Lymphomas	1.5	1.4	1.3	1.4	1.3	1.2
Reticuloendothelial neoplasms	0.6	0.5	0.4	0.5	0.5	0.4
CNS tumours	2.0	2.2	2.2	2.3	2.3	1.7
Tumours of the sympathetical nervous system	1.1	1.1	1.2	1.0	1.0	0.9
Retinoblastoma	0.4	0.3	0.4	0.3	0.4	0.2
Kidney tumours	1.0	0.8	0.9	0.9	0.8	0.7
Bone tumours	0.7	0.6	0.6	0.6	0.6	0.5
Soft tissue tumours	0.8	0.8	0.8	0.8	0.9	0.8
Germ cell tumours	0.6	0.5	0.5	0.3	0.5	0.4
All malignancies	13.2	13.0	13.0	12.8	12.9	11.1

to establish contact with general practitioners or other physicians who are in contact with the patients. After the patients have grown up, they have to be asked to give their own informed consent for further data storage in the registry and long-term follow-up. So far, our experience on whether this will function well over a long time period is limited.

Long-time follow-up is of special importance because of possible late effects which may be partly related to treatment modalities. To date, we have been able to trace more than 300 secondary malignancies. Finally, studies of offspring will also be performed.

In the present paper, follow-up data have only been used for global survival analyses. Using the large amount of clinical data which are also stored in the registry, additional analyses, e.g. according to clinical stage or other relevant risk factors, can be performed. In this way, survival analyses which are carried out within clinical trials may be compared with analyses which relate to the general population.

In comparing the German registry with foreign ones, it has to be taken into account that our present data refer to a later time period than was available for the other registries in the study by Parkin and colleagues [2]. We selected the later time period because, in the first years of our registry, the registration was less complete than that of other registries, many of which had existed for many years.

In addition to the descriptive analysis of the registry data, which is routinely presented in annual reports, the registry now forms the basis for analytical epidemiological studies. Future work will be increasingly related to the conduct of such studies.

Since 1991, the cases of the eastern region of Germany have also been included in the registry. Here, completeness of notification possibly still has to be improved. With complete data from the total F.R.G., the registry will become the largest registry of childhood malignancies. This is the first time we have prepared a comprehensive paper describing our registry in an international journal, it should be a reference document for descriptive epidemiology of childhood cancer, and we are willing to make our data available for all people interested in this. Because childhood malignancies are very rare, increased international co-operation is needed in the future in order to explore specific questions in more detail.

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Metachronous Pulmonary Metastases Resection in Patients With Ewing's Sarcoma Initially Treated With Adjuvant or Neoadjuvant Chemotherapy

G. Bacci, A. Briccoli, P. Picci and S. Ferrari

55 patients with Ewing's sarcoma of bone, treated at our Institution with adjuvant or neoadjuvant chemotherapy between 1972 and 1990, relapsed with pulmonary metastases alone. 12 of these patients—selected according to their long disease-free interval before relapse, monolaterality of the lesions, small numbers of metastatic nodules, resectability and refusal to undergo further chemotherapic treatments—were treated with surgical resection of the metastatic lesions and with no additional radio- or chemotherapy. At a follow-up ranging between 3 and 14 years (mean 9 years), 5 of these 12 patients (42%), were continuously free of disease, whereas the remaining 7 patients died with uncontrolled disease 12–39 months (mean 22 months) after thoracotomy. These results seem to indicate that an aggressive surgical approach should be considered for a selected group of Ewing's sarcoma patients who relapse with only lung metastases.

Key words: Ewing's sarcoma, pulmonary metastases, surgery, survival
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INTRODUCTION

ADJUVANT AND neoadjuvant chemotherapy have dramatically improved the prognosis for patients with Ewing's sarcoma of bone. However, approximately 40% of these patients eventually develop metastases, which in almost half the cases are initially located only in the lung [1–3].

Several treatments have recently been attempted for these patients: a combination of cytotoxic drugs [4, 5], a high dose of melphalan associated with bone marrow transplantation [6], and half-body irradiation [7]. Although some of these therapies gave an initial response, very few patients (less than 10%) were eventually cured. The role of surgery in the treatment of pulmonary metastases from Ewing's sarcoma has so far, been neglected. We are aware of only one paper in which 19 cases were retrospectively evaluated [8].

The purpose of this paper is to report the results achieved at our Institution between 1979 and 1991 in 12 selected patients who, after having been initially treated with adjuvant or neoadjuvant chemotherapy for a Ewing's sarcoma of bone, relapsed with lung metastases alone and were treated with surgical resection of the pulmonary lesions.

MATERIALS AND METHODS

Among the 316 patients with Ewing's sarcoma of bone treated at the Rizzoli Institute between 1972 and 1990 with adjuvant (144 cases) or neoadjuvant (172 cases) chemotherapy [9, 10], 125 relapsed with metastatic disease, which in 45 cases was located only in the lung. 12 of these patients were treated with pulmonary resections, whereas the remaining 33 received additional chemotherapy, in 10 cases associated with radiotherapy. No attempt was made to differentiate Ewing's sarcoma from primary neuroectodermal tumour (PNET).

The decision to perform surgical treatment instead of chemo-

Correspondence S. Ferrari.
S. Ferrari and G. Bacci are at the Sezione di Chemioterapia dei Tumori Ossei, Istituto Ortopedico Rizzoli, Via Pupilli 1, 40136 Bologna; A. Briccoli is at the Patologia Chirurgica dell'Università di Modena; and P. Picci is at the Laboratorio Ricerca Oncologica cell'Istituto Rizzoli, Italy.
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