available at www.sciencedirect.com

SCIENCE DIRECT®

journal homepage: www.ejconline.com

Bone tumours in European children and adolescents, 1978–1997. Report from the Automated Childhood Cancer Information System project

C.A. Stiller[a,*], S.S. Bielack[b,c], G. Jundt[d], E. Steliarova-Foucher[e]

[a]Childhood Cancer Research Group, Department of Paediatrics, University of Oxford, 57 Woodstock Road, Oxford OX2 6HJ, UK
[b]Paediatrics 5 (Haematology, Oncology, Immunology), Olgahospital, Stuttgart, Germany
[c]University Children's Hospital Münster, Department of Paediatric Haematology and Oncology, Münster, Germany
[d]Basel Cancer Registry and Bone Tumour Reference Centre at the Institute of Pathology, University Hospital Basel, Basel, Switzerland
[e]Descriptive Epidemiology Group, International Agency for Research on Cancer, Lyon, France

ARTICLE INFO

Keywords:
Childhood cancer
Adolescent
Bone neoplasms
Osteosarcoma
Ewing's sarcoma
Europe
Epidemiology
Incidence
Survival
Registry

ABSTRACT

Data on 5572 children and adolescents diagnosed with malignant bone tumours (International Classification of Childhood Cancer, Group VIII) before the age of 20 years during 1978–1997 in Europe were extracted from the Automated Childhood Cancer Information System (ACCIS) database. Age-standardised incidence among children during the period 1988–1997 was similar for boys and girls aged 0–14 years (5.5–5.6 per million). Among adolescents aged 15–19 years, males had higher incidence (19.3 per million) than females (10.7 per million). Among children, osteosarcoma accounted for 51% of registrations and Ewing's sarcoma for 41%. Among adolescents, 55% of registrations were osteosarcoma and 28% Ewing's sarcoma. Both tumours had their highest incidence in late childhood or early adolescence. There were no significant time trends in incidence during 1978–1997. Five-year survival estimates for patients diagnosed during 1988–1997 were, respectively, 59% and 51% among children and adolescents with osteosarcoma and 62% and 30% among children and adolescents with Ewing's sarcoma. Between 1978–1982 and 1993–1997, survival increased for both children and adolescents with osteosarcoma, and for children with Ewing's sarcoma.

1. Introduction

Malignant bone tumours account for 3–5% of cancers diagnosed in children under 15 years of age[1] and 7–8% of those in adolescents aged 15–19 years in western populations.[2] Malignant bone tumours comprise more than 20 different entities, classified according to either the direct product of the tumour cells (e.g. osteoid in osteosarcomas) or the type of tissue they form (e.g. vascular channels in angiosarcoma of bone).[3] The great majority of malignant bone tumours occurring in young people under the age of 20 years are osteosarcoma and Ewing's sarcoma. Most malignant bone tumours, including both of these types, must be regarded as high-grade sarcomas that, at the time of diagnosis, are likely to have spread to distant sites, especially the lungs. In the pre-chemotherapeutic era, their prognosis was very poor, since treatment was focussed on local procedures.

Identified risk factors for osteosarcoma are limited to ionising radiation, e.g. radiotherapy for a previous cancer, and certain genetic conditions including familial retinoblastoma,

* *Corresponding author*: Tel.: +44 1865 315925; fax: +44 1865 315940.
E-mail addresses: charles.stiller@ccrg.ox.ac.uk, charles.stiller@ccrg.oxford.ac.uk (C.A. Stiller).
0959-8049/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejca.2006.05.015

Li-Fraumeni syndrome and Rothmund-Thomson syndrome.[4,5] Ewing's sarcoma has long been known to have lower incidence among black and East Asian populations,[6] indicating that genetic factors may be important in its aetiology. Cytogenetic differences between Ewing's tumours from European and Japanese patients lend further support to this suggestion.[7] Analyses of combined data from several case-control studies in North America and Australia have confirmed earlier findings of a raised risk with a history of umbilical hernia, possibly with a common environmental cause,[8] and with parental occupation in farming, though with no indication of the relative importance of exposure to particular categories of chemicals or animals.[9]

This paper presents geographical patterns and time trends in the incidence and survival rates for malignant bone tumours among children and adolescents in Europe and identifies needs for further studies. The analyses are based on a large European database within the Automated Childhood Cancer Information System (ACCIS), which contains data from 80 population-based cancer registries in 35 participating countries.[10]

2. Material and methods

Malignant bone tumours were defined as all those neoplasms in group VIII of the International Classification of Childhood Cancer (ICCC).[11] All 5572 malignant bone tumours registered since 1978 in patients under 20 years of age in 59 participating cancer registries of 19 European countries were extracted from the ACCIS database (Table 1). This number included 2883 osteosarcomas (ICCC subgroup VIIIa), 231 chondrosarcomas (ICCC subgroup VIIIb), 2130 Ewing's sarcomas (ICCC subgroup VIIIc), 165 other specified malignant tumours (ICCC subgroup VIIId) and 163 unspecified tumours (ICCC subgroup VIIIe). Information available for each case included basic demographic data (age, sex, country or region of residence), information on the tumour (date of incidence, site, morphology, basis of diagnosis and laterality) and on follow-up (date of last contact and vital status). Detailed information on the database is given elsewhere [Steliarova-Foucher, Kaatsch, Lacour, and colleagues, this issue].

The selected cancer registries (Table 1) met defined quality criteria for completeness, validity and comparability [Steliarova-Foucher, Kaatsch, Lacour, and colleagues, this issue]. Table 1 shows the numbers of cases and indicators of data quality for each set of analyses. In nearly all the registries, more than 95% of cases were microscopically verified and, among those registries with access to mortality data, fewer than 1% were registered from death certificate only (DCO).

The contributing countries were grouped into five European regions according to geographical location, socioeconomic characteristics and data availability, as shown in Table 1. The underlying population at risk for each combination of registration area, calendar year, sex and single year of age was extracted, where available, from official statistics and otherwise was estimated by linear interpolation from available data [Steliarova-Foucher, Kaatsch, Lacour, and colleagues, this issue]. Only in the Northern region did all contributing registries provide data for the full age range 0–19 years. In all the other regions, substantial numbers of cases came from paediatric registries that did not cover adolescents aged 15–19 years.

For the analyses of time trends, the available time-span was divided into four periods of 5 years: 1978–1982, 1983–1987, 1988–1992 and 1993–1997. The registries contributing to the analyses of time trends were those covering at least three periods, as shown in Table 1. Quality indicators for the combined data included in the analyses of time trends are shown in Table 2, by time period and geographical region.

Incidence rates were calculated as the average annual number of cases per million person-years. Age-standardised rates (ASR) were calculated from the age-specific incidence rates for 5-year age groups weighted according to the World standard population. Variations in incidence between the five European regions were analysed by Poisson regression. Time trends in incidence were evaluated using Poisson regression, adjusted for sex, age and region as appropriate, and expressed as an average annual percentage change (AAPC).

The duration of survival for each case was calculated as the time elapsed between the date of diagnosis and the date of death (if the patient died) or closing date of the study for the given cancer registry. Survival rates were analysed using the life-table method. DCO cases and those without follow-up were excluded from the survival analyses. The extent of these exclusions can be evaluated from Tables 1 and 2. Variations in survival between groups of patients were tested by log-rank tests.[12] More details on the methods used can be found elsewhere [Steliarova-Foucher, Kaatsch, Lacour, and colleagues, this issue]. To assess differences in survival between children and adolescents we analysed data from the restricted set of registries covering the whole age range 0–19 years.

3. Results

Table 3 shows incidence of bone tumours during 1988–1997 by 5-year age group among males and females in Europe as a whole, and Fig. 1 shows incidence by single year of age. Osteosarcoma was the most frequent subgroup, accounting for 52% of all registrations. Ewing's sarcoma was second most frequent, accounting for 34%. Chondrosarcoma and other specified tumours accounted for 6% and 4%, respectively, and 4% of registrations were for tumours of unspecified type. All types of bone tumour were very rare before the age of 4 years (Fig. 1). For all bone tumours combined, and for osteosarcoma, Ewing's sarcoma and chondrosarcoma, incidence increased with age until a peak in late childhood or adolescence and then declined. Incidence rates for all subgroups were similar for boys and girls throughout childhood (Table 3, Fig. 1). Incidence of osteosarcoma reached a marked peak at age 15 years among males, however, and remained higher than among females thereafter. Incidence of Ewing's sarcoma among males was slightly higher at age 15–18 years than at 11–14 years, starting to decline only at age 19 years (Fig. 1), whereas among females the incidence was substantially lower than in late childhood (Table 3, Fig. 1). In consequence, incidence rates for all bone tumours combined were similar for males and females during childhood, whereas there was a pronounced male excess among adolescents (Fig. 1).