Original Research

Geographical variability in survival of European children with central nervous system tumours

G. Gatta a,*, R. Peris-Bonet b, O. Visser c, C. Stiller d, R. Marcos-Gragera e, M.-J. Sánchez f,g, B. Lacour h,i, P. Kaatsch j, F. Berrino k, S. Rutkowsky l, L. Botta a, and the EUROCARE-5 Working Group

a Evaluative Epidemiology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
b Spanish Registry of Childhood Tumours (RETI-SEHOP), Universidad de Valencia, Valencia, Spain
c Netherlands Comprehensive Cancer Organization, Utrecht, The Netherlands
e Epidemiology Unit and Girona Cancer Registry, Oncology Coordination Plan, Department of Health, Government of Catalonia, Catalan Institute of Oncology, Girona, Spain
f Escuela Andaluza de Salud Pública, Instituto de Investigación Biosanitaria ibs, Granada, Hospitales Universitarios de Granada/Universidad de Granada, Granada, Spain
g CIBER de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
h French National Registry of Childhood Solid Tumours, CHU, Nancy, France
i INSERM, UMRS-1153, CRESS Team 7, University of Paris-Sorbonne, Paris, France
j German Childhood Cancer Registry, Institute for Medical Biostatistics, Epidemiology and Informatics, University of Mainz, Mainz, Germany
k Department of Preventive and Predictive Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
l Department of Pediatric Haematology and Oncology, University Medical Center Hamburg-Eppendorf, Germany

Received 16 January 2017; received in revised form 11 May 2017; accepted 16 May 2017

KEYWORDS
Childhood cancer survival;

Abstract Survival for childhood central nervous system (CNS) tumours varies across Europe, partly because of the difficulty of distinguishing malignant from non-malignant disease. This study examines bias in CNS tumours survival analysis to obtain the reliable and comparable survival figures.
We analysed survival data for about 15,000 children (age <15) diagnosed with CNS between 2000 and 2007, from 71 population-based cancer registries in 27 countries. We selected high-quality data based on registry-specific data quality indicators and recorded observed 1-year and 5-year survival by countries and CNS entity.

We provided age-adjusted survival and used a Cox model to calculate the hazard ratios (HRs) of death, adjusting by age, site and grading by country.

Recording of non-malignant lesions, use of appropriate morphology codes and completeness of life status follow-up differed among registries. Five-year survival by countries varied less when non-malignant tumours were included, with rates between 79.5% and 42.8%. The HRs of dying, for registries with good data, adjusting by age and grading, were between 0.7 and 1.2; differences were similar when site (supra- and infra-tentorial) was included.

Several sources of bias affect the correct definition of CNS tumours, the completeness of incidence series and the goodness of follow-up. The European Network of Cancer Registries needs to improve childhood cancer registration and stress the need to update the International Classification for Cancer. Since survival differences persisted even when restricting the analysis to registries with satisfactory data, and since diagnosis of CNS tumours is difficult and treatment complex, national plans must aim for the revision of the diagnosis and the coordination of care, with adequate national and international networks.

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1. Introduction

The central nervous system (CNS) is the most common site of solid tumours affecting children [1]. Five-year survival of children with malignant CNS tumours in Europe in 2005–2007 was 58%, from 54% in Eastern regions and the UK and Ireland to 65% in the North [2]. There is presumably ample room for improvement in regions with low survival. However, data on CNS tumours collected by European population-based cancer registries (CRs) are not completely comparable. In a previous analysis of European childhood cancer survival, the differences in registration criteria were so extensive that CNS tumours had to be removed from the analysis of all childhood cancers combined for reliable comparison of survival across countries [2].

We analysed the main sources of bias in childhood CNS tumour survival across Europe, considering the completeness of incidence series, standardisation of the definition of disease entities, the collection and completeness of benign and borderline lesions, and the quality of follow-up. The major aim was to produce more reliable survival figures for CNS tumours by country, eliminating as far as possible biases affecting comparisons, to illustrate survival variability between countries.

2. Materials and methods

2.1. Study design and data collection

The EUROCARE-5 database [2] covers about 38,000 CNS tumours, defined as group III in the International Classification of Childhood Cancers, third edition (ICCC-3) [3], diagnosed in European children aged 0–14 years from 1-Jan-1978 to 31-Dec-2007, with vital status updated to 31-Dec-2008. We obtained data from 71 population-based CRs in 27 countries (Table 1). Most countries had national cancer registration. All registries sent data for anonymous central analysis according to a standardised protocol [4].

Tumours were grouped into the six categories defined by ICCC-3, group III [3,5]. The EUROCARE-5 protocol [4] asked registries to include both malignant tumours (5th digit in the morphology code equal to 3 in the International Classification of Diseases for Oncology third edition, ICD-O M) and tumours with non-malignant behaviour (5th digit in the morphology codes: 0 or 1). However, some registries communicated to have an incomplete collection of non-malignant tumours (Austria, Bulgaria, Finland, Latvia, Lithuania and Poland).

To analyse survival differences between countries, we had to check the quality of data. For CNS tumour, most important indicators of data quality were: the proportions of unspecified intracranial and intraspinal neoplasms—ICCC-3-IIIf; the proportion of glioma NOS (M-9380/2-3, excluding optical nerve); the proportion of non-malignant tumours, which may suggest, if too low, incomplete registration; the 5-year survival of CNS tumours with very bad prognosis—atypical teratoid/rhabdoid tumours (M-9508/3), anaplastic astrocytoma (M-9401/3), anaplastic oligodendroglioma (M-9451/3) and glioblastoma (M-9440/3-9442/3) which, if higher than average, suggests errors in follow-up.

2.2. Data analysis

Observed survival was calculated by the actuarial method. Survival was analysed on a data set containing