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RESEARCH ARTICLE

Cancer in children and adolescents in Spain: incidence, treatment setting and provider specialty

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Abstract

Purpose To analyze cancer incidence, distribution of malignancy, treatment setting and provider specialty of cancer patients, 0–19 years old, in the Comunitat Valenciana, Spain.

Methods/patients All incident childhood and adolescent (0–19 years) cancer cases registered in the population-based Comunitat Valenciana Childhood Cancer Registry (RTICV) from 2007 to 2010 were included. Pathological and hematological diagnoses were recoded using the International Classification of Childhood Cancer Third Edition (ICCC-3). Treatment setting and provider specialty were analyzed.

Results 696 patients <20 years were diagnosed with cancer: 513 cases were children (0–14 years) and 183 were adolescents (15–19 years). Overall age-adjusted incidence for 2007–2010 was 176.0 cases per million (95 % CI 162.8–189.2), with incidence being the highest among infants (287.4), followed by 1–4 years (205.5), adolescents (179.9), 10–14 years (150.2) and 5–9 years (140.6). Among adolescents aged 14–19 years, the treatment setting differed by cancer type; 87 % of them were never seen at pediatric oncology units, while 40 % were treated in up to 20 different medical oncology departments in institutions without pediatric oncology expertise.

Conclusions This is the first population-based epidemiological study carried out in Spain on children and adolescents with cancer. Centralization of care to a small number of specialized centers and thorough pediatric and oncology team collaboration are needed to improve care and survival for adolescents with cancer in our country. We suggest the creation of specific adolescent tumor boards in main tertiary care hospitals, in which adolescents with cancer can benefit from the shared expertise of medical and pediatric specialists.

Keywords Population-based cancer registries · Cancer incidence · Treatment setting · Children · Adolescent · Spain

Introduction

Adolescents are a unique age group, with patterns of disease and healthcare challenges distinctly different than those faced by younger children and adults. Teenagers from 15 to 19 do not only have a higher overall incidence of malignancy than children, but also a different disease distribution to children and adults [1–4]. Unlike younger or older patients, adolescents may be referred by pediatricians/general physicians to either pediatric or adult oncologists. A definitive association between treatment setting and outcome in this group of patients has not yet been established. However, recent data suggest that adolescents with cancer are not treated at optimal settings, enrolled in clinical trials at low rates and, for certain tumor types, outcome may be better when care is delivered in a pediatric center or according to a pediatric protocol [5–7].

Approximately 400–450 adolescents aged 15–19 years are estimated to be diagnosed with cancer each year in

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Spain based on the incidence rate in Europe and the 15–19 years old population in Spain [3, 8, 9]; however, no real incidence data are available in our country. Most patients treated in Spanish pediatric oncology centers are usually registered in the Spanish Childhood Cancer Registry (RETI-SEHOP). The RETI-SEHOP is a hospital-based cancer registry that collects cases from all Spanish pediatric oncology centers and covers the entire country, with an estimated average completeness of 90 % in the 0–14 years old group [10]. However, concerning the 15–19 years old group, there is an important lack of information regarding cancer incidence, pattern of referral, treatment setting and provider specialty. Spain is divided in 17 regions (Autonomous Communities) and the pediatric age cutoff ranges from 14 to 18 years old not just among different regions but also among different hospitals within the same community.

Comunitat Valenciana is one of the seventeen regions in Spain. It is located in the east coast and covers a total population of 5.1 million, including ca. 1 million children and adolescents which represents 11 % of the 0–19 years old population in Spain [9] (Fig. 1). The Comunitat Valenciana Childhood Cancer Registry (RTICV) is the only population-based childhood & teenager cancer registry in Spain. It depends on the Public Health Directorate General, Health Department of Valencian Government and collects childhood cancer data (0–14 years) since 1983, as well as adolescent data (15–19 years) since 2007 covering 100 % of the Comunitat Valenciana population.

Our objective is to determine the incidence, distribution of malignancy, treatment setting and provider specialty of cancer patients 0–19 years old in the Comunitat Valenciana, with the aim to estimate adolescent cancer incidence in our region and to compare their demographic, disease and clinical characteristics according to treatment setting and provider specialty.

Methods

For the purpose of this study, all incident childhood and adolescent (0–19 years) cancer cases registered in the Comunitat Valenciana Childhood Cancer Registry (RTICV) from 2007 to 2010 were included. Residence status was determined through insurance card and, if available, identity card, as well as confirmed through systematic review of medical records. Non-resident cancer cases at the time of diagnosis were excluded.

Individual pathological and hematological diagnoses were reviewed and recoded using the International Classification of Childhood Cancer Third Edition (ICCC-3) into 12 main diagnosis groups [11]. RTICV usually identifies incident cases of cancer through routine and systematic review of pathology reports, medical records, radiation therapy records and hospital discharge list from the 21 public and 5 private hospitals in our region. Estimate of completeness of case coverage was of 98 % during the study period. Annually, information of cases treated in all hospitals of the CV is requested, and identified patients are compared with the database generated with cases from previous years. The information on possible cases is verified and completed by consulting medical history, and contrasted with the demographics of the Population Information System and Mortality Registry. Indicators of data quality of the Registry in this period were: 94.7 % microscopic verification (MV), 0 % Death Certificate Only (DCO) registrations; and 0.03 % cases with unspecified histology in subgroups and 0 % with unspecified histology in group diagnostic.

Treatment setting and provider specialty were also retrospectively analyzed. Data were provided anonymized by the RTICV and therefore considered exempt of the ethics panel.

Standard variables for each case included demographic data (birth date, age, sex, residence at diagnosis) and

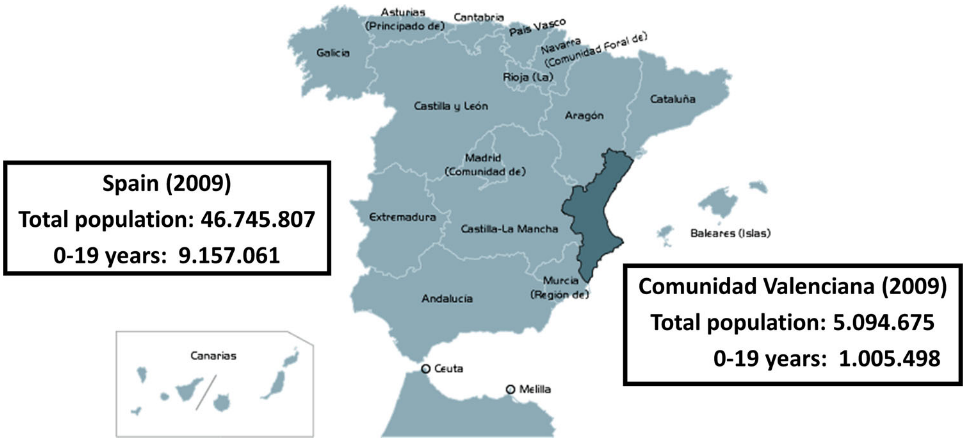

Fig. 1 Spain and the Comunitat Valenciana, National Statistics Institute (2007–2010)

clinical data (diagnosis date, ICCC-3 diagnostic group), provider specialty (pediatric vs medical oncologist) and treatment setting. The population at risk in the period was 3.964.716 person-years, obtained from the National Statistics Institute [9]. Based on the pediatric age cutoff in our region, patients were grouped in two (<14 and ≥14 years) for treatment setting and provider specialty analysis. For incidence and distribution of malignancy analysis, the usual age grouping was employed (0, 1–4, 5–9, 10–14 and 15–19 years). In our region there are 21 public and 5 private medical oncology services, as well as three public pediatric oncology units. All three pediatric oncology units have pediatric oncologists/surgeons on staff and are located within a tertiary care hospital with full access to appropriate pediatric subspecialties and pediatric supportive care. For this analysis, different centers of treatment were aggregated into the following groups: (1) Pediatric Oncology Center, (2) Medical Oncology Center with a pediatric oncology center within the same institution, (3) Medical Oncology Center without a pediatric oncology center within the same institution.

Statistical analysis

Incidence rates were calculated by specific age groups and crude rate for all groups by sex and adjusted standardized rates by world population. Categorical variables were described with the numerical count (percentage) of each category and 95 % confidence intervals (CI). Categorical variables were compared using Chi-squared test. $p < 0.05$ was considered as statistically significant. Data were analyzed using SPSS 20.0 and Epidat 3.1.

Results

From January 2007 to December 2010, there were 696 patients younger than 20 years, residents in the Comunitat Valenciana and diagnosed with a new cancer. Five hundred and thirteen cases were children between 0 and 14 years old and 183 were adolescents between 15 and 19 years. Diagnosis was microscopically verified in 94.7 % of cases.

Overall age-adjusted incidence for 2007–2010 was 176.0 cases per million (95 % CI 162.8–189.2), with incidence being the highest among infants (287.4), followed by 1–4 years (205.5), adolescents (179.9), 10–14 years (150.2) and 5–9 years (140.6). In children (0–14 years) leukemia was the most common diagnosis, followed by CNS tumors, lymphomas, bone tumors and neuroblastoma. In adolescents (15–19 years), lymphoma was the most common diagnosis, followed by CNS tumors, leukemia, other carcinomas/melanomas and bone and germ cell tumors (Table 1).

A total of 499 patients were treated at pediatric oncology units (72 %; 95 % CI 68–75 %). The proportion of patients treated at a pediatric oncology center declined with age (Fig. 2). Nearly all children younger than 14 years old with cancer received their oncology care at a pediatric oncology unit, while only 57 % (95 % CI 39–75 %) of 14-year-olds and 4 % (95 % CI 1–7 %) of 15–19-year-olds ($p = 0.001$) (Table 2), Accordingly, 14 years of age has been considered the cutoff point for the analysis of treatment setting and provider specialty in our cohort.

Only 13 % (95 % CI 8–17 %) of ≥14 years old were treated in Pediatric Oncology Units; 47 % (95 % CI 40–54 %) were treated at Medical Oncology Departments with a pediatric oncology unit within the same institution whereas 40 % (95 % CI 34–47 %) at a Medical Oncology Department without.

Regarding different centers of treatment 60 % (95 % CI 53–67 %) of 14–19-year-olds were treated in one of the three main tertiary care hospitals of the Comunitat Valenciana (whether in the pediatric or medical oncology center), while 40 % (95 % CI 34–47 %) were treated in one of the remaining 20 different medical oncology departments (median 4 patients/4 years period, range 1–15 patients). The percentage of 14–19-year-olds treated in one of the three main tertiary care hospitals in the Comunitat Valenciana increased from 56 % (95 % CI 42–69 %) in 2007 up to 72 % (95 % CI 59–85 %) in 2010 ($p = 0.17$). Among adolescents aged 14–19 years, the treatment setting differed by diagnostic (Table 2). When compared by diagnostic category, malignancies such as leukemia and bone and soft tissue sarcomas were more frequently treated in one of the three main tertiary care hospitals (whether in the pediatric or medical oncology center), than malignancies such as germ cell tumors and other carcinomas/melanomas ($p = 0.001$),

Discussion

This is the first population-based epidemiological study carried out in Spain on adolescents with cancer. The data presented come from the only population-based specialized childhood and teenager cancer registry in Spain, RTICV, which covers 100 % of the 0–19-year-olds of the Comunitat Valenciana population [12]. Population-based cancer registries, such as the RTICV, record all new cases in a geographically defined area, independently of provider specialty, and are thus unique for monitoring cancer incidence and provide indicators for planning and evaluating cancer control activities [12, 13].

In our study, 513 patients were ≤14 years at cancer diagnosis and 183 were between 15 and 19 years. Childhood and adolescent cancer incidence is similar to

Table 1 Cancer incidence age-standardized rate (ASRw) per million person-years in the Comunitat Valenciana (2007–2010) by age groups according to the ICCC-3

Diagnostic group (ICCC-3)	0 years old	1–4 years old	5–9 years old	10–14 years old	15–19 years old	ASRw (95 % CI)
I. Leukemias	55.5	76.0	51.3	22.4	27.7	45.7 (38.9–52.5)
II. Lymphomas	10.1	16.6	16.4	29.8	45.5	25.6 (20.7–30.5)
III. CNS neoplasms	40.3	36.8	39.0	33.0	33.6	36.0 (30.1–42.0)
IV. Neuroblastoma	70.6	28.5	2.1	1.1	1.0	12.1 (8.4–15.7)
V. Retinoblastoma	15.1	7.1	1.0	0.0	0.0	2.9 (1.1–4.7)
VI. Renal tumors	20.2	17.8	4.1	1.1	0.0	6.8 (4.0–9.5)
VII. Liver tumors	20.2	3.6	0.0	1.1	1.0	2.5 (0.9–4.2)
VIII. Bone tumors	0.0	3.6	11.3	30.9	19.8	15.1 (11.3–18.8)
IX. Soft tissue sarcoma	25.2	10.7	10.3	7.5	8.9	10.3 (7.1–13.5)
X. Germ cell tumors	15.1	3.6	1.0	9.6	16.8	8.0 (5.2–10.7)
XI. Other carcinomas/melanomas	15.1	1.2	4.1	13.8	25.7	11.1 (7.9–14.3)
Total	287.4	205.5	140.6	150.2	179.9	176.0 (162.8–189.2)

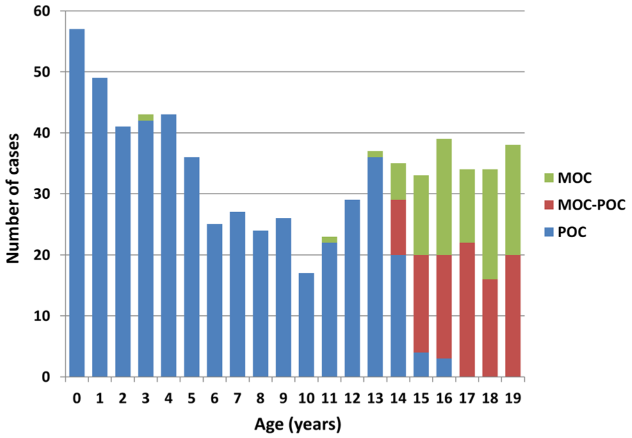

Fig. 2 Site of care for cancer patients in the Comunitat Valenciana by age (2007–2010). *POC* Pediatric Oncology Center, *MOC-POC* Medical Oncology Center with a Pediatric Oncology Center within the same institution, *MOC* Medical Oncology Center without a Pediatric Oncology Center within the same institution

previously described with higher overall incidence of malignancy in adolescents than in children. [3, 14, 15]. Nearly all children younger than 14 years old with cancer received their oncology care at a pediatric oncology unit, whereas only 4 % of 15–19-year-olds was treated at pediatric units compared to 30–47 % in other countries [16–19]. This decline in utilization of pediatric units is explained by the current pediatric age cutoff (14 years old) in the Comunitat Valenciana as well as in most Spanish regions.

Cancer in adolescents represents a transition between the non-epithelial types common during childhood and the epithelial types that account for most cancers in adults [1–4, 14]. Compared to younger or older patients, adolescents may be referred to pediatric or adult oncologists depending on referral physician and/or center of treatment policy. This unique pattern of disease and pattern of referral means that few institutions develop the required expertise, infrastructure or clinical trial opportunities for better management of the adolescents with cancer.

In our study, while 60 % of 14–19-year-olds were treated in the three main tertiary care hospitals (within the pediatric or medical center), 40 % were treated in one of the remaining 20 different medical oncology departments. For this study, only the main treatment center was recorded and therefore the number of treating centers per patient cannot be presented. The type of cancer had a strong influence on site of care: those more common during childhood such as leukemia and bone/soft tissue sarcomas were mostly centralized in one of the three main tertiary care hospitals, whereas those more common during adulthood such as germ cell tumors and other carcinomas/melanomas were independently referred to medical oncology departments. Multiple treatment centers and lack of pediatric cancer expertise within the same institution (not only oncologists and surgeons, but pathologists, radiologists, etc.) may hamper access to best cancer diagnosis and treatment for this group of patients.

Different international consensuses emphasize the importance of specialized care and clearly state that “all care for children and young people under 19 years old must be provided in age-appropriate facilities”, “must have access to tumor-specific or treatment-specific clinical expertise”, “be offered entry to any clinical research trial for which they are eligible” and “treated according to the best available treatment protocol” [20, 21]. In order to achieve these aims, centralization of care of adolescents with cancer, as already successfully achieved for children,

Table 2 Site of care for 14–19-year-olds with cancer in the Comunitat Valenciana (2007–2010) by diagnosis

	14 years				15–19 years			
	POC	MOC-POC	MOC	Total	POC	MOC-POC	MOC	Total
I. Leukemias	2	0	0	2	5	21	2	28
II. Lymphomas	6	0	1	7	0	22	25	47
III. CNS Neoplasms	4	3	2	9	0	20	14	34
IV. Neuroblastoma	0	0	0	0	0	1	0	1
V. Retinoblastoma	0	0	0	0	0	0	0	0
VI. Renal tumors	0	0	0	0	0	0	0	0
VII. Liver tumors	1	0	0	1	0	1	0	1
VIII. Bone tumors	3	0	3	6	1	16	3	20
IX. Soft tissue sarcoma	2	0	1	3	1	3	5	9
X. Germ cell tumors	2	0	0	2	0	4	13	17
XI. Other carcinomas/melanomas	0	3	2	5	0	8	18	26
Total	20	6	9	35	7	96	80	183

POC Pediatric Oncology Center, *MOC-POC* Medical Oncology Center with a Pediatric Oncology Center within the same institution, *MOC* Medical Oncology Center without a Pediatric Oncology Center within the same institution

will surely improve their care and outcome. This could be achieved through specific teenager and young adult (TYA) cancer centers or integration into current pediatric and/or medical oncology departments. It is worth noting, that in our study, the proportion of adolescents treated at one the three main tertiary care hospitals has clearly been increasing (56 % in 2007, 72 % in 2010), although statistically not significant.

Adolescents treated in pediatric oncology centers are more likely to be enrolled in clinical trials than those who receive their care elsewhere. The lower rate of trial enrollment in this age group is probably responsible, at least in part, of the insufficient improvement in survival, morbidity and quality of life among adolescents compared with children or adults [7]. As most adult clinical trials usually have a lower age limit of 18 years [22], what happens with 14–17-year-olds treated at medical oncology institutions? Collaboration between pediatric and adult oncology teams throughout specific adolescent programs can improve the sharing of expertise and clinical trial enrollment, as shown by the AYA Oncology Program in Pittsburg [23].

In Spain, a new National Strategic Plan for Childhood and Adolescence [24] has recently recommended the extension of current pediatric upper age cutoff to 18 years, facilitating treatment of adolescents in fewer, pediatric units. Nevertheless, current decentralized health care system in our country will hinder the accomplishment of this Plan and advances will have to be achieved at the regional level.

Our study has several limitations. On one hand, due to the usual delay of population-based cancer registries, the last year analyzed in our study is 2010 and may no longer reflect the current situation. RTICV is a population-based registry that needs information of cases treated in all hospitals of the CV in order to verify the cases. However, some hospitals do not provide their data in a timely manner. Nevertheless, as the only new regulatory modification introduced (National Strategic Plan for Childhood and Adolescent [24]) is still not implemented in our region and the pediatric age cutoff has therefore not changed, the data presented still reflect the real situation in our region. Another limitation is that although provider specialty and treatment setting were analyzed, actual degree of collaboration between pediatric and adult specialists could not be retrospectively assessed: some medical oncology departments without pediatric oncology expertise may have consulted with pediatric specialists, while some pediatric and adult specialists within the same institution may have never discussed their adolescent patients. Neither time to diagnosis nor care pathways could be retrospectively assessed. Although distance to cancer treatment was not analyzed in this study, we do not think that the distance between the patient's home and the nearest pediatric oncology center plays a major role, since in all cases they can be reached in less than 2 h by car.

In summary, we have found that most 14–19 years old with cancer in the Comunitat Valenciana in the 2007–2010 period were not seen at pediatric oncology units and almost half of them were treated in institutions without pediatric oncology expertise. Centralization of care to a small number of specialized centers and thorough pediatric and oncology team collaboration are needed to improve care and survival for adolescents with cancer. We suggest the creation of specific adolescent tumor boards in main tertiary care hospitals, in which adolescents with cancer can benefit from the shared expertise of medical and pediatric specialists.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Informed consent Data were provided anonymized by the Comunitat Valenciana Childhood Cancer Registry (RTICV) and therefore considered exempt of the ethics panel. The RTICV belongs to the Public Health Directorate General, Health Department of Valencian Government. For this type of study, formal consent is not required.

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