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Cancer mortality among adolescents and young adults: A historical cohort in a reference institution for cancer treatment in Santa Catarina/South of Brazil 2002–2013

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ABSTRACT

Objective: To identify factors associated with early mortality from cancer in adolescents and young adults in a reference institution for oncology treatment in Santa Catarina, Brazil.
Methods: We studied a retrospective cohort with an intentional sample of adolescents (ages 15–19) and young adults (ages 20–29) diagnosed with neoplasia. Secondary data were acquired from January 2002 to December 2013. Kaplan–Meier and Cox regression methods were used for survival analysis. Logistical analysis tested the association between early death (lower tertile between diagnosis and death, according to cancer type) and clinical or sociodemographic variables.
Results: We included a total of 889 cases with an average age of 23, with similar gender distributions and a predominance of Caucasian ethnicity. Using the Cox framework of proportional risks adjusted for neoplasia types and gender, individuals with non-hematological neoplasia (solid tumors) presented a 47% higher risk of dying when compared with individuals diagnosed with leukemias and lymphomas (HR: 1.47; 95%CI: 1.12–1.93). Chances of death were 31% higher for males than for females (HR: 1.31; 95% CI: 1.02–1.69). When adjusting for type of neoplasia and age (15–24 and 25–29) the risk of death by cancer was 51% greater in individuals diagnosed with non-hematological neoplasia when compared with individuals diagnosed with leukemias and lymphomas (HR: 1.51; 95%CI: 1.15–1.99). The chance of death by cancer in patients under the age of 25 was 33% greater when compared to that in older patients between the ages of 25 and 29 (HR: 1.33; 95%CI: 1.04–1.75). In multiple regression analysis, factors associated with early mortality from cancer were the number of years in school ($P = 0.011$) and time between diagnosis and start of treatment ($P < 0.001$).
Conclusions: The sample studied with a longer period of time between diagnosis and the start of treatment (access to oncology therapy) and with fewer years in school showed that these factors had important roles in early death from cancer for the observed individuals. This must be considered when planning and identifying risk in young cancer patients in order to lower the impact of the disease on mortality for this age group.

1. Introduction

Cancer represents a set of over 200 different diseases which have in common the disorderly proliferation of cells, a majority of which have invasive potential. Unlike cancers in children (individuals up to 14 years of age) and adults (individuals over age 30), those in adolescents and young adults (AYAs) differ in their main locations (topography), morphological and histological aspects, genetic profiles, and clinical behaviors. This must be considered in therapy choices – as well as in psychosocial and sociocultural aspects unique to this age group – for the best evolution possible [1–3].

Among other factors related to difficulties in early diagnosis and detection for this group are: (a) lack of clear and reliable information to understand tumor biology; (b) an elevated sense of invincibility in young adults and adolescents; (c) low suspicion of cancer diagnosis by health professionals; and (d) reduced number of primary care services and specialized infrastructures for

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this population [4]. All of these factors could directly and negatively influence treatment, survival and mortality for this population.

Epidemiological studies on AYA cancer are lacking in the specialized literature. If they exist, they are difficult to interpret, particularly because of inadequate samples (representing approximately 5% of all neoplasias), limited numbers of publications (often presenting data analyzed in tandem with younger and older groups), information heterogeneity (from the definition of the studied population to histological and topographic classifications), as well as differences and inadequacies in data collection and the recording of cancers [5].

In spite of advances in technological and therapeutic modalities for cancer treatment, particularly in the last decades, there is no evidence of mortality rates diminishing for adolescents and young adults. This goes against data found for other age groups – for example the pediatric group (ages 0–14) – for the same types of cancer [6–8]. In developed countries such as the United States, Canada, the United Kingdom, France, and even Brazil, cancer represents the main cause of death among young adults and adolescents, without considering external causes (accidents and violence) [9–14].

The knowledge of the epidemiological profile and aspects associated with mortality from cancer allows for a better understanding of the natural history of this group of diseases, favoring policies for prevention and early diagnosis, therapy advances, and consequent increases in survival.

This study aims to determine social, economic, and clinical factors associated with "early death" in young adults and adolescents with cancer – controlled by type of neoplasia, gender, and age – in patients in a reference institution for oncology treatment in Santa Catarina, Brazil.

2. Methods

The retrospective cohort with an intentional sample of adolescents (ages 15–19) and young adults (ages 20–29) with a diagnosis of neoplasia used secondary data from a public-domain database, the information system of hospital cancer records (Sistema de Informações de Registro Hospitalar de Câncer, SisRHC), complemented by records from a high-complexity assistance unit in oncology (Centro de Pesquisas Oncológicas de Santa Catarina, CEPON) between January 2002 and December 2013.

CEPON provides outpatient services, admission, emergency care, oncology support, palliative care, radiotherapy, complementary exams (imaging and pathology), and multidisciplinary services exclusively dedicated to patients under the Brazilian healthcare system (Sistema Único de Saúde, SUS). Under international guidelines for AYA cancer patient healthcare and in accordance with nationwide guidelines, CEPON created a service for young adults and adolescents (Serviço de Adolescentes e Jovens Adultos, AJAS/CEPON) in 2013. By the year 2012, AYAs with cancer were treated exclusively by clinical oncologists. From 2013, with the creation of AJAS, patients were treated by a mixed team (pediatric oncologists and clinical oncologists).

Data obtained from SisRHC/CEPON and from a system database on mortality (Sistema de Informações sobre Mortalidade, SIM) were complementarily allocated in an Excel® spreadsheet (Microsoft Office® for Mac 2016, Radmond/WA, USA) for organization. Variables utilized were: age, gender, ethnicity, length of time in school, city of birth, histological type, neoplasia type, staging, primary care clinic, first line of treatment performed, family history of cancer, smoking habits, drinking habits, and death by cancer. The STATA® software (STATA/SE® 14 for Mac, College Station/TX, USA) was used to perform all statistical analyses.

Tumors staged according to the TNM staging system (UICC, 6th edition) were classified as metastatic in stage IV. Other tumors staged due to other classifications were considered "metastatic" with distant disease (stages IVa and IVb in the Ann Arbor rating for Hodgkin and non-Hodgkin lymphomas, and stage IV in the FIGO rating for ovarian tumors). Primary tumors in the central nervous system were not considered in this study.

The non-parametric Kaplan–Meier method (with and without stratification) and the Cox regression method were used for survival analysis [15,16].

Survival was considered as the time between diagnosis and death from cancer, calculated in months. For all analyses, "time zero" was considered as the date of diagnosis and the final event was death from cancer. Individuals who died from other causes unrelated to the studied disease (cancer) were excluded from the study before analysis. Survival curves among different categories within the same independent variable (age groups, for example) were compared via log-rank test. The semi-parametric framework for proportional risks by Cox was used to estimate risk ratios for neoplasia and histological types, adjusted for gender and age; associations with $P < 0.05$ were considered significant. Residue analysis was performed to assess global framework adjustment.

The "early death" closure was considered for logistical analysis, characterized by the occurrence of the lower tertile in time between diagnosis and death, according to each type of cancer. This was performed in order to control the effect of each cancer type during its evolution time, and also to assess the association between early death and sociodemographic or clinical variables in the entire sample as a single group. This was necessary since the sample included a great variety of cancers, which made isolated stratified analyses non-viable.

Bivariance analyses used the chi-squared test, considering associations presenting $P < 0.05$ as significant. Independent associations were tested with a theoretical framework based on literature data on the topic using multiple regression with forward selection at each stage, with the Hosmer–Lemeshow adjustment quality index being used to assess framework sturdiness. Associations presenting $P < 0.05$ were considered significant.

This project was not eligible for assessment by the Ethics Committee for Research in Human Beings as it was a historical cohort study using secondary databases, without making use of interviews, questionnaires, or other types of human involvement. CEPON granted this study access to its RHC database on September 22nd 2015 via a letter of permission sent by its head director.

3. Results

From the total of 1242 cases within RHC/CEPON between 2002 and 2013, 290 cases were ignored as they presented one or more of the following situations: (a) confirmed cancer diagnosis with first line of treatment performed at another institution; (b) confirmed cancer diagnosis treated at another institution, visit to CEPON being only for clinical assessment, symptomatic treatment, or palliative care; (c) confirmed cancer diagnosis forwarded to another institution for treatment; and (d) relapse or second neoplasia of surviving infant cancer patients. Cases without a start date for treatment (n = 22) were also ignored due to the impossibility of calculating the time between diagnosis and the beginning of treatment. Other cases ignored were deaths from other causes (n = 41). Table 1 summarizes the sociodemographic and clinical characteristics of the cohort.

The average age observed was 23 years (standard deviation = 4.27 years). From the 889 cases eligible for analysis, 509 (57.3%) entered the institution at ages 15–24, and 380 (42.7%) presented at