Early Second Malignant Neoplasms (SMN) in Pediatric Oncology Patients: A National Population Based study

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(on behalf of study team)

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Excellent survival outcomes in pediatric cancer patients

- OS at 5 years: >80%

SEER registry data

Survivorship

- A range of treatment related short term and long term adverse effects

- Second Malignant neoplasms (SMN) is a well recognized complication

SMN

- Large data available on long term incidence and outcomes of SMNs in pediatric oncology patients

- Data available from many different countries in Europe: National Registries

Second malignant neoplasms after childhood cancer: A nationwide population-based study in Korea

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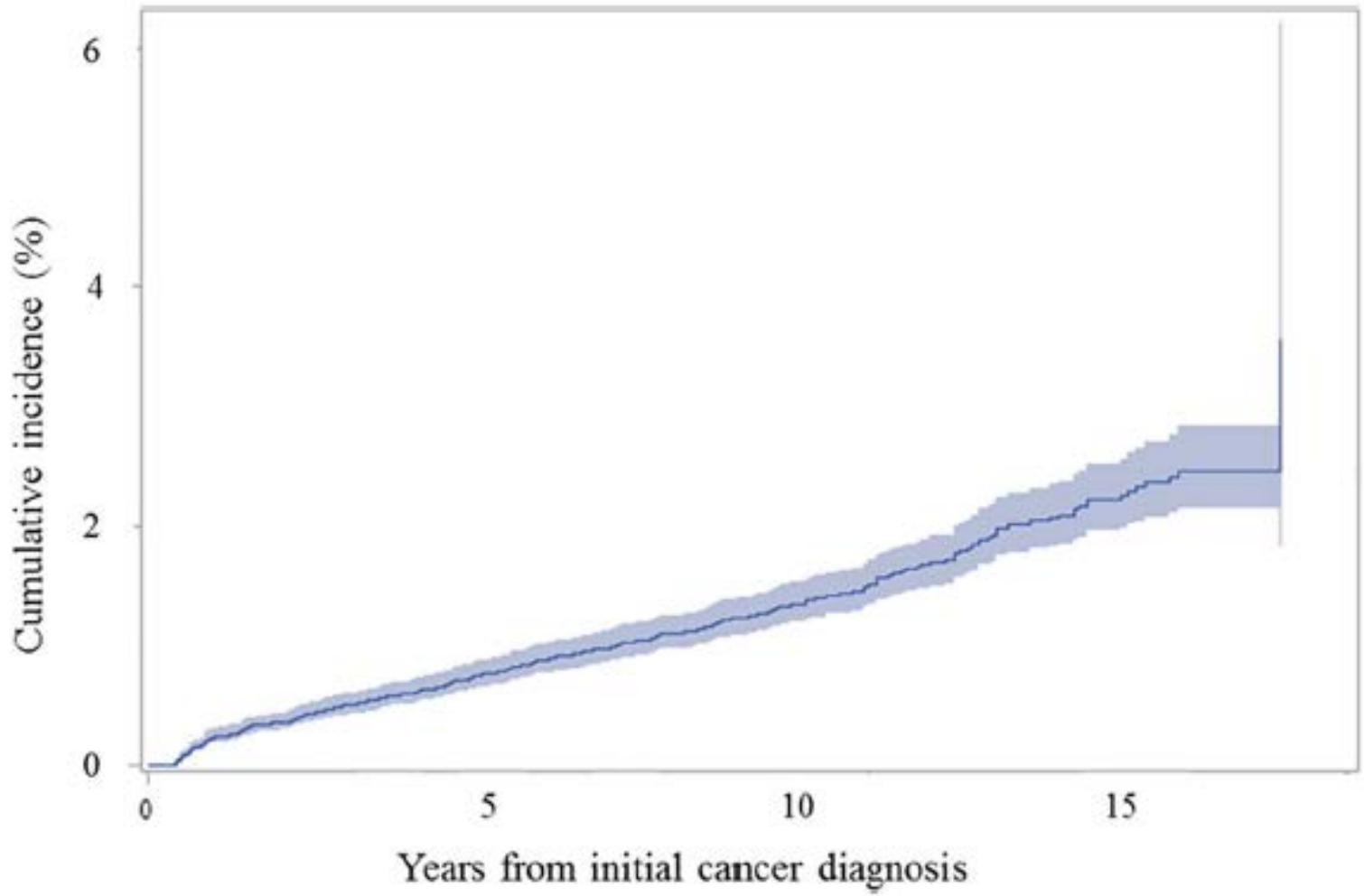
Cumulative incidence (%)
6
4
2
0
0
5
10
15
Years from initial cancer diagnosis

SMN

- Large cohorts:
  - ALL
  - Germ cell tumors
  - Non-CNS tumors
  - Many other tumors

  - More recently *AYA*

Keegan et al, JAMA Oncol. 2017 Nov; 3(11): 1554–1557; Nygaard et al, Acta Paediatr Scand. 1991 Dec;80(12):1220-8. Casagranda et al, Pediatr Hematol Oncol. 2016 Sep;33(6):371-382. Epub 2016 Sep 29. Li et al, Int J Neurosci. 2017 Nov;127(11):1005-1011.

Paucity of data form Canada

Subsequent Malignant Neoplasms in a Population-Based Cohort of Pediatric Cancer Patients: A Focus on the First 5 Years

Jason D. Pole[1,2], Lan Ying Gu[3], Victoria Kirsh[2,3], Mark L. Greenberg[1,4,5], and Paul C. Nathan[4]

Cancer Epidemiol Biomarkers Prev; 24(10) October 2015

Limitations of current literature

- Few national data on all cancer types: population based
- Little data on early SMNs (within 5 years of treatment)
- Modelling for risk factors
- Limited data on management outcome of SMN

Current study

- SIOP 2017: Meeting of CYPC research champions
- Several potential studies discussed
- Current study was first conceived at this meeting

Study

Incidence, characteristics and outcomes of subsequent primary malignancies within 5 years of diagnosis in pediatric cancer patients in Canada

The process

- Preliminary proposal
- Call for interest
- Core group identified
- Study meetings

Current investigators: Core Group

- Jason Pole
- Ketan Kulkarni
- Lillian Sung
- Marie-Claude Pelland-Marcotte
- Noelle Cullinan
- Randy Barber
- Sapna Oberoi
- Samuele Renzi
- Sara Israels
- Thai Hoa Tran
- PHAC (Dianne Zakaria; Lin Xie)

Aim

- The aim of the present study is to assess the incidence, characteristics, management and outcome of children who developed SMN malignancies within 5 years of diagnosis of their first cancer.

- A secondary aim is to assess the risk factors associated with development of SMN within 5 years of diagnosis.

Methods

- Study design: Retrospective population based cohort study

- Patients with SMN will be identified from the Cancer in Young People – Canada (CYP-C) national pediatric cancer registry among all patients diagnosed with their first cancer from 2001-2015 inclusive

Inclusion Criteria

- All patients diagnosed with a primary malignancy from 0 to <15 years of age will be included in the study.

SMN: Definition

- Any patient who developed a SMN that is histologically or morphologically distinct form the primary cancer within 5 years of diagnosis will be included for analysis.

Variables included

- Patient demographics: age (in months), gender
- Diagnosis and management:
  - diagnosis type
  - age in months at initial and subsequent diagnoses
  - date of diagnosis
  - management (chemotherapy with individual drug doses, radiotherapy, surgery, bone marrow transplant)
  - outcome (survival, death, relapse, progression)
  - genetics information of the participants and malignancies will be assessed (as available)

Variables included

- Comparison with control data:
  - Demographic characteristics
  - cancer diagnosis
  - underlying genetic diagnoses (if any)
  - therapy (chemotherapy, surgery and radiation)

Statistical Analysis

- PHAC supporting analysis for this study

PHAC Mandate

- The data custodians of CYP-C, the Public Health Agency of Canada (PHAC), has a mandate to analyze and publish data from CYP-C for the purposes of routine and enhanced public health surveillance and epidemiology.

- PHAC is seeking external collaborators with expertise in pediatric oncology who are interested in working on impactful manuscripts.

Statistical analysis

- The number of person-years at risk will be calculated for the entire cohort as the time from the date of primary diagnosis until the earliest of the second malignant neoplasms diagnosis, death, or the end of the follow-up period.

- A cumulative incidence curve for the development of SMN will be generated with death treated as a competing risk.

Statistical analysis

- SIRs will be calculated by calculating the ratio of the observed number of SMN to the expected incident cancers, derived from age- and sex-specific Canada population cancer incidence data from Statistics Canada.

- A series of models that examine factors associated with the development of an SMN will be developed using a proportional hazards approach utilizing the person-years at risk described above.

Statistical analysis

- OS and EFS for patients with (and without SMN) will be generated using Kaplan Meyer survival curves

Anticipated results

- The present data will accurately document the incidence of early SMN within 5 years of initial diagnosis in children aged 0 to <15 years from Canada over the last 15 years.

- The data will be able to establish the characteristics, management and outcome of these patients.

- Risk factors for SMN will be assessed.

Limitations

- CYPC includes follow up data for 5 years after diagnosis: No data on late SMN
- Age >14 excluded
- Statistical power: expected n=300
- Linkage with other registries

Significance of data

- This will be the first national study assessing the incidence, characteristics, risk factors and outcome of early SMN in Canadian children from age 0 to <15 from 2001-2015.

- The results can aid in highlighting the patients at high risk for developing second and subsequent malignancies and make specific recommendations for management and care of these patients.

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  - PHAC

THANK YOU