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Original Research

Long-term risk of renal and urinary tract diseases in childhood cancer survivors: A population-based cohort study



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KEYWORDS

Childhood cancer; Survivorship; Late complications; Renal diseases; Urinary tract diseases Abstract *Background:* Childhood cancer has been associated with long-term risk of urinary tract diseases, but risk patterns remain to be comprehensively investigated. We analysed the lifetime risk of urinary tract diseases in survivors of childhood cancer in the Nordic countries. *Methods:* We identified 32,519 one-year survivors of childhood cancer diagnosed since the 1940s and 1950s in the five Nordic cancer registries and selected 211,156 population comparisons of a corresponding age, sex, and country of residence from the national population registries. To obtain information on all first-time hospitalizations for a urinary tract disease, we linked all study subjects to the national hospital registry of each country. Relative risks (RRs) and absolute excess risks (AERs) and associated 95% confidence intervals (CIs) for urinary tract diseases among cancer survivors were calculated with the appropriate morbidity rates among comparisons as reference.

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Results: We observed 1645 childhood cancer survivors ever hospitalized for urinary tract disease yielding an RR of 2.5 (95% CI 2.4–2.7) and an AER of 229 (95% CI 210–248) per 100,000 person-years. The cumulative risk at age 60 was 22% in cancer survivors and 10% in comparisons. Infections of the urinary system and chronic kidney disease showed the highest excess risks, whereas survivors of neuroblastoma, hepatic and renal tumours experienced the highest RRs.

Conclusion: Survivors of childhood cancer had an excess risk of urinary tract diseases and for most diseases the risk remained elevated throughout life. The highest risks occurred following therapy of childhood abdominal tumours.

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1. Introduction

Remarkable improvements in therapy for paediatric malignancies have led to an increasing number of adults treated for cancer during childhood. In the Nordic countries, 5-year survival rates after childhood cancer now exceed 80% [1] and almost 1 in 1000 adults in the general population is a childhood cancer survivor [2]. However, a considerable number of survivors experience long-term therapy-related complications [3,4]. Only few and relatively small studies are available on the risk of diseases of the urinary tract following treatment for childhood cancer [5,6]. Important contributors to renal damage are nephrotoxic chemotherapy, nephrectomy, and abdominal irradiation [7]. The St. Jude Lifetime Cohort Study reported kidney dysfunction in 5% of adult cancer survivors [8]. The aim of this study was to identify urinary tract diseases through long-term follow-up in a large cohort of childhood cancer survivors in the five Nordic countries. To measure the relative and absolute risk of urinary tract morbidities we used diagnostic information available in the national hospital registers including risk estimates for individuals aged >50 years which have not previously been reported in cohort studies of childhood cancer survivors.

2. Methods

This study is part of a Nordic population-based cohort study, Adult Life after Childhood Cancer in Scandinavia (ALiCCS; www.aliccs.org) [9–11].

2.1. Patient and comparison cohorts

The basic childhood cancer cohort included 43,909 individuals diagnosed with cancer before the age of 20 years from start of registration in the 1940s and 1950s, until 31st December 2008 (eTable1). Patients had to be alive on or born after the date on which centralised registration of residents of each country was operational to be included. The Nordic cancer registries include

nationwide data on incident cases of cancer reported from multiple sources ensuring close to full coverage [12–16]. We obtained information on type of cancer and date of diagnosis and assigned individuals to 1 of 12 main diagnostic groups according to the International Classification Scheme for Childhood Cancer [17].

All residents in the Nordic countries are assigned a unique personal identification number, which allows accurate linkage of information between registries and complete follow-up on vital status and emigration [18].

To measure hospitalization rates for urinary tract diseases in the background population, we randomly selected 219,131 comparison subjects from the population registries (eTable 1). For each childhood cancer patient, five comparisons were selected, who were alive on the date of cancer diagnosis of the corresponding patient, and were of the same sex, age, country of residence, and without a diagnosis of cancer before the age of 20 years. For 317 patients fewer than five comparisons were available (eFig. 1).

Patients, in whom more than one primary cancer was diagnosed before the age of 20 years, were excluded (305 patients). Furthermore, we excluded those who had died, emigrated, or were censored during the first year after the date of cancer diagnosis or an equivalent time lag for the comparisons (6844 patients; 1318 comparisons). We also excluded those who had died or emigrated before the start of the national hospital registries (3600 patients; 4858 comparisons).

In accordance with Nordic regulations, data on cohort members were analysed without personal identifiers. The study was approved by the national bioethics committees and national data protection authorities according to national regulations.

2.2. Hospitalizations for urinary tract diseases

Each hospitalization obtained from the national hospital registries initiated a record including the personal identification number of the patient, date of admission and discharge, a primary discharge diagnosis, and supplementary diagnoses coded according to the

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