

ENGLISH SUMMARY

Survival of childhood cancer has improved enormously in the past half century, from a five-year survival of 20% in the 1950s and 60s to one of more than 80% today. The improved survival has led to a steadily growing population of survivors, and an increased awareness of the many long-term effects of cancer treatment.

Thus, an improved survival comes at a price. To varying degrees, these former patients may experience a wide spectrum of complications caused by the life-saving treatment, from insignificant and treatable ones to severe permanent damage, or even to life-threatening and fatal. Among the major sequelae are impaired growth and development, chronic morbidity, reproductive difficulties, second cancers and increased mortality. However, the late effect pattern, especially that seen decades after ended treatment, is not yet fully described.

The main objectives of the studies included in this thesis were to investigate serious late effects of childhood cancer. Among the leading non-malignant causes of death among survivors are cardiovascular- and respiratory diseases, and late infections. We, therefore, aimed to investigate hospitalization for these outcomes in a large population-based cohort of Nordic childhood cancer survivors, using discharge diagnoses from national hospital registries. The Nordic countries are ideal for this type of epidemiological research due to public use of unique personal identification numbers (PIN) assigned to all citizens. The PINs ensure complete follow-up of study subjects and reliable linkage between the many high-quality health registries of the Nordic countries.

The population-based studies presented in this thesis are among the first large studies describing the detailed patterns of hospitalizations for all types of cardiovascular-, respiratory- and infectious diseases lifelong in childhood cancer survivors and population comparisons, with the exclusive use of medically verified outcome diagnoses. More than 21,000 survivors and 150,000 population comparisons were followed for these outcomes in the national hospital registries of the Nordic countries. The observed number of first-time hospitalizations for a given outcome in survivors was compared with that expected, derived from the disease rate in the population comparison cohort, and the standardized hospitalization rate ratio (RR) and absolute excess risk (AER) of the outcomes were calculated.

Survivors had an increased risk of hospitalization for all outcomes studied, i.e. approximately a two-fold increased relative risk of cardiovascular disease,

respiratory disease, and infections. For each additional year of follow-up approximately 3, 9 and 6 out of 1000 survivors were hospitalized with a new excess cardiovascular-, respiratory- and infectious disease, respectively. Although the latter figures are reassuring to a certain degree, these excess risks persisted throughout life. The pattern of excess hospitalizations among survivors was predominated by cerebrovascular disease, acute respiratory infections, and bacterial infections. The pattern of morbidity was highly dependent on the type of childhood cancer, generally with the highest risks seen in survivors of Hodgkin lymphoma, leukemia, hepatic tumors and neuroblastoma.

Medical professionals must be aware of the increased risks and the complexity of the possible late effects survivors of childhood cancers may face. Our findings further emphasize the importance of following survivors in specialized clinics, in addition to the continuously updated evidence-based follow-up guidelines. Survivors themselves also need to be aware of their increased risks, and it is important to urge the survivors to adopt a healthy, non-smoking lifestyle.

As the population of survivors continues to grow, so does the importance of knowing what can be expected. Cure is not enough, and after all, our goal is to ensure that all survivors experience a life as long and healthy as possible.