



Late surgical intervention after childhood cancer treatment

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“Late effects” is a very well-qualified term as it encompasses the range of physical, mental and social consequences of cancer treatment. Over the past several decades in North America, multimodal cancer therapies such as high-dose anticancer drugs, high-dose local irradiation, hematopoietic stem cell transplantation and active surgeries have been developed to improve treatment outcomes for childhood cancer to the 5-year survival rate with nearly 85% (1). However, the chronic health problems of long-term survivors, namely the enormous late effects, have become a problem and have come to be emphasized (2). In particular, the mortality rate increases with secondary cancers and with increasing age. Dieffenbach and North American pediatric oncologists have analyzed the frequency and content of surgeries performed among childhood cancer survivors (CCS), comparing them with their siblings (3). The study involves 31 institutions across the United States, including Boston Children’s Hospital, the first in the world to treat childhood leukemia, and St. Jude Hospital, a world leader in CCS research. The cohort was more than 25,000 long-term CCS with a median follow-up of 22.2 years. These long-term, large-scale follow-up data, as well as comparisons with siblings sharing genetic and lifestyle backgrounds, have a very strong impact on their results. Readers will be keenly aware of the need for keeping a system for long-term follow-up of CCS together with their siblings, even in countries such as Japan that are following Europe and

the United States in terms of treatment. In this study, a late surgical intervention was defined as any surgical procedure requiring general or monitored anesthesia performed more than 5 years after initial cancer diagnosis. They use the mean cumulative counts (MCCs) to quantify and compare the cumulative number of late surgical interventions (4). As a result, the cumulative number of post-diagnosis surgical interventions was graphed for each disease, and a comparison with siblings was successfully presented in a very easy-to-understand manner.

Survivors of Hodgkin’s lymphoma (HL), Ewing’s sarcoma, and osteosarcoma had the highest MCC of late surgeries (333.3, 322.9, and 269.6 per 100 survivors). High rates of late central nervous system (CNS) surgeries were identified among survivors of CNS malignancies. Cardiovascular, breast and endocrine surgery for HL and spinal surgery for neuroblastoma were common. And late musculoskeletal surgeries were performed at a high rate among Ewing sarcoma survivors and osteosarcoma survivors. Breast, cardiovascular, and endocrine surgical interventions were common among female HL survivors. It was also notable that female survivors had higher rates of late major surgery than did males. In addition, the results of this analysis are characterized by an increased rate of major late surgery among survivors diagnosed in the 1990s compared with survivors in the 1970s. A major limitation of this paper may be that these late surgical interventions were

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estimated from self-reported data, and dropouts and over-reporting might have affected the assessment of cumulative numbers.

Recently, with the introduction of new antibody-drug conjugate brentuximab vedotin for the treatment of HL (5), the role of irradiation has been greatly reduced. Long-term survivors of HL diagnosed in the 2020s could be expected to undergo fewer late surgical interventions, but how about Ewing sarcoma? We hope similar analyzes could be reported about the recent CCS in the future. Finally, I would like to thank Dr. Jun Okamura for thinking about this comment together.

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appropriately investigated and resolved.

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